WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Tuesday, August 23, 2005

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L21	L19 and pancrea?	1
☐	L20	L2L19 and gemcitabine	0
☐	L19	L2 and antibod?	6
☐	L18	L13 and L15	3
☐	L17	L13 and chemotherap?	12
☐	L16	L15 and gemcitabine	1
☐	L15	L13 and Her-2/neu	3
☐	L14	L13 and herceptin	1
☐	L13	L12 with donald.inv.	25
☐	L12	buchsbaum.inv.	167
☐	L11	L10 and chemo?	0
☐	L10	L8 and radiation	2
☐	L9	L8 and chemotherapeut?	0
☐	L8	Her-2/neu receptor antibod?	2
☐	L7	L2 and gemcitabine	3
☐	L6	L2 and chemotherapeu?	0
☐	L5	L2 with gemcitabine	0
☐	L4	L2 with cisplatin	0
☐	L3	L2 with chemotherapeu?	0
☐	L2	L1 with her-2/neu receptor	6
☐	L1	herceptin	1181

END OF SEARCH HISTORY

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Tuesday, August 23, 2005

Hide?	Set Name	Query	Hit Count
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☐	L27	L26 and pancrea?	16
☐	L26	L25 and colon	40
☐	L25	L24 and gemcitabine	45
☐	L24	L22 and herceptin	129
☐	L23	L22 and Her-2/neu receptor?	3
☐	L22	tumors with growth factor receptors	2072
☐	L21	L19 and pancrea?	1
☐	L20	L2L19 and gemcitabine	0
☐	L19	L2 and antibod?	6
☐	L18	L13 and L15	3
☐	L17	L13 and chemotherap?	12
☐	L16	L15 and gemcitabine	1
☐	L15	L13 and Her-2/neu	3
☐	L14	L13 and herceptin	1
☐	L13	L12 with donald.inv.	25
☐	L12	buchsbaum.inv.	167
☐	L11	L10 and chemo?	0
☐	L10	L8 and radiation	2
☐	L9	L8 and chemotherapeut?	0
☐	L8	Her-2/neu receptor antibod?	2
☐	L7	L2 and gemcitabine	3
☐	L6	L2 and chemotherapeu?	0
☐	L5	L2 with gemcitabine	0
☐	L4	L2 with cisplatin	0
☐	L3	L2 with chemotherapeu?	0
☐	L2	L1 with her-2/neu receptor	6
☐	L1	herceptin	1181

END OF SEARCH HISTORY

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     FILE 'HCAPLUS' ENTERED AT 13:39:18 ON 23 AUG 2005
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                  "BUCHSBAUM DONALD J"/AU OR "BUCHSBAUM DONALD JAY"/AU)
L2             26 SEA ABB=ON  L1 AND ?GROWTH?(W)?FACTOR?
L3             10 SEA ABB=ON  L2 AND ?RADIAT?
L4                ANALYZE L3 6 CT :       13 TERMS

     FILE 'REGISTRY' ENTERED AT 13:47:58 ON 23 AUG 2005
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L5              1 SEA ABB=ON  HERCEPTIN/CN
                  E HER-2/NEU/CN
L7              4 SEA ABB=ON  (PACLITAXEL OR GEMCITABINE OR 5-FLUOROURACIL OR
                  DOXORUBICIN)/CN

     FILE 'HCAPLUS' ENTERED AT 13:49:05 ON 23 AUG 2005
L8           1154 SEA ABB=ON  (L5 OR ?HERCEPTIN? OR HER-2/NEU)
L9           2811 SEA ABB=ON  (L5 OR ?HERCEPTIN? OR HER-2)
L10          2070 SEA ABB=ON  L9 AND ?RECEPT?
L11           950 SEA ABB=ON  L10 AND ?ANTIBOD?
L12           186 SEA ABB=ON  L11 AND (L7 OR ?PACLITAXEL? OR ?GEMCITABINE? OR
                  5(W)?FLUOROURACIL? OR ?DOXORUBIXIN?)
L13            65 SEA ABB=ON  L12 AND (?CANCER? OR ?CARCIN? OR ?NEOPLASM? OR
                  ?TUMOR? OR ?TUMOUR?)(3A)(?PANCR? OR ?COLON?)
L14             1 SEA ABB=ON  L13 AND HER(W)2(W)NEU

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 13:53:12 ON
     23 AUG 2005
L15             2 SEA ABB=ON  L14
L16             2 DUP REMOV L15 (0 DUPLICATES REMOVED)  2 cite from above d.b.'s

     FILE 'USPATFULL' ENTERED AT 13:54:22 ON 23 AUG 2005
L17           245 SEA ABB=ON  L13 AND HER(W)2(W)NEU
L18           152 SEA ABB=ON  L17 AND (PRD<20011207  OR PD<20011207)
L19             2 SEA ABB=ON  L18 AND ?COMB?(W)?RADIAT?  2 cite from uspatfull

     FILE 'HCAPLUS' ENTERED AT 13:57:43 ON 23 AUG 2005
L20            65 SEA ABB=ON  L13 OR L14
L21            35 SEA ABB=ON  L20 AND (PRD<20011207 OR PD<20011207)
L22             1 SEA ABB=ON  L21 AND ?COMB?(W)?RADIAT?
L23             3 SEA ABB=ON  L21 AND ?RADIAT?
L24            35 SEA ABB=ON  L21 OR L22 OR L23  35 cite from CAPlus

     FILE HOME

     FILE HCAPLUS

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FILE COVERS 1907 - 23 Aug 2005 VOL 143 ISS 9
FILE LAST UPDATED: 22 Aug 2005 (20050822/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 AUG 2005 HIGHEST RN 861291-85-2
DICTIONARY FILE UPDATES: 22 AUG 2005 HIGHEST RN 861291-85-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE MEDLINE
FILE LAST UPDATED: 20 AUG 2005 (20050820/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 17 August 2005 (20050817/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 18 Aug 2005 (20050818/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE JAPIO
FILE LAST UPDATED: 2 AUG 2005 <20050802/UP>
FILE COVERS APR 1973 TO APRIL 28, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS
FILE COVERS 1985 TO 22 AUG 2005 (20050822/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED
TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 23 Aug 2005 (20050823/PD)
FILE LAST UPDATED: 23 Aug 2005 (20050823/ED)
HIGHEST GRANTED PATENT NUMBER: US6934966
HIGHEST APPLICATION PUBLICATION NUMBER: US2005183181
CA INDEXING IS CURRENT THROUGH 23 Aug 2005 (20050823/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 23 Aug 2005 (20050823/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

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>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate

substance identification.

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L7             4 SEA FILE=REGISTRY ABB=ON  (PACLITAXEL OR GEMCITABINE OR
                 5-FLUOROURACIL OR DOXORUBICIN)/CN
L9          2811 SEA FILE=HCAPLUS ABB=ON  (L5 OR ?HERCEPTIN? OR HER-2)
L10         2070 SEA FILE=HCAPLUS ABB=ON  L9 AND ?RECEPT?
L11          950 SEA FILE=HCAPLUS ABB=ON  L10 AND ?ANTIBOD?
L12          186 SEA FILE=HCAPLUS ABB=ON  L11 AND (L7 OR ?PACLITAXEL? OR
                 ?GEMCITABINE? OR 5(W)?FLUOROURACIL? OR ?DOXORUBIXIN?)
L13           65 SEA FILE=HCAPLUS ABB=ON  L12 AND (?CANCER? OR ?CARCIN? OR
                 ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)(3A)(?PANCR? OR ?COLON?)
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L20           65 SEA FILE=HCAPLUS ABB=ON  L13 OR L14
L21           35 SEA FILE=HCAPLUS ABB=ON  L20 AND (PRD<20011207 OR PD<20011207)
L22            1 SEA FILE=HCAPLUS ABB=ON  L21 AND ?COMB?(W)?RADIAT?
L23            3 SEA FILE=HCAPLUS ABB=ON  L21 AND ?RADIAT?
L24           35 SEA FILE=HCAPLUS ABB=ON  L21 OR L22 OR L23

=> d ibib abs 124 1-35

L24  ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:902199  HCAPLUS
DOCUMENT NUMBER:          141:374704
TITLE:                    Composition and uses of galectin antagonists to
                          augment treatment of cancer or other proliferative
                          disorders
INVENTOR(S):              Chang, Yan; Sasak, Vodek
PATENT ASSIGNEE(S):       Glycogenesys, Inc., USA
SOURCE:                   PCT Int. Appl., 51 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004091634         A1    20041028    WO 2004-US10675         20040407
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     US 2004023925         A1    20040205    US 2003-408723          20030407 <--
     US 2004223971         A1    20041111    US 2004-819901          20040407
PRIORITY APPLN. INFO.:                       US 2003-408723       A  20030407
                                             US 2003-461006P      P  20030407
                                             US 2003-474562P      P  20030530
                                             US 2001-299991P      P  20010621 <--
                                             US 2002-176235       A2 20020620
AB   The present invention is directed to methods and compns. for augmenting
     treatment of cancers and other proliferative disorders.  In particular
     embodiments, the invention combines the administration of an agent that
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inhibits the anti-apoptotic activity of galectin-3 (e.g., a 'galectin-3 inhibitor') so as to potentiate the toxicity of a chemotherapeutic agent. In certain preferred embodiments, the conjoint therapies of the present invention can be used to improve the efficacy of those chemotherapeutic agents whose cytotoxicity is influenced by the status of an anti-apoptotic Bcl-2 protein for the treated cell. For instance, galectin-3 inhibitors can be administered in combination with a chemotherapeutic agent that interferes with DNA replication fidelity or cell-cycle progression of cells undergoing unwanted proliferation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:559502 HCAPLUS
DOCUMENT NUMBER: 141:190802
TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors
INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin, John J.; Li, Ge; Huang, Chia-yu; James, Ray A.; Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish A.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 731 pp., Cont.-in-part of U.S. Ser. No. 85,896.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 2004122018	A1	20040624	US 2002-325896		20021219	<--
US 2002198216	A1	20021226	US 2001-940811		20010828	<--
US 2003229099	A1	20031211	US 2002-85896		20020227	<--
US 2004122018	A1	20040624	US 2002-325896		20021219	<--
PRIORITY APPLN. INFO.:			US 2001-940811	A2	20010828	<--
			US 2002-85896	A2	20020227	
			US 2002-325896	A	20021219	
			US 2000-229183P	P	20000830	<--

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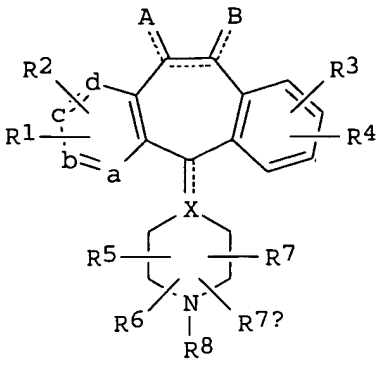

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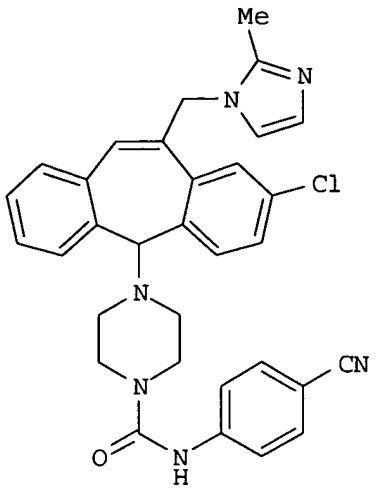

II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

L24 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:559501 HCAPLUS

DOCUMENT NUMBER: 141:106498

TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors

INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin, John J.; Li, Ge; Huang, Chia-yu; James, Ray A.; Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 731 pp., Cont.-in-part of U.S. Ser. No. 85,896.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004122018	A1	20040624	US 2002-325896	20021219 <--
US 2002198216	A1	20021226	US 2001-940811	20010828 <--
US 2003229099	A1	20031211	US 2002-85896	20020227 <--
US 2004122018	A1	20040624	US 2002-325896	20021219 <--

PRIORITY APPLN. INFO.:
US 2001-940811 A2 20010828 <--
US 2002-85896 A2 20020227
US 2002-325896 A 20021219
US 2000-229183P P 20000830 <--

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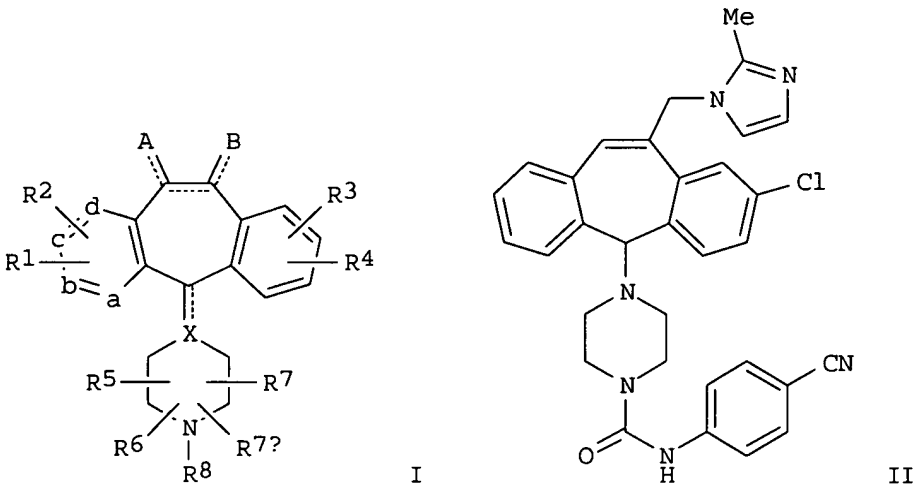

I II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention

inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

L24 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:533970 HCAPLUS
DOCUMENT NUMBER: 141:65088
TITLE: Methods and compositions for the prevention or treatment of neoplasia comprising a COX-2 inhibitor in combination with an epidermal growth factor **receptor** antagonist
INVENTOR(S): Masferrer, Jaime
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 470,951.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004127470	A1	20040701	US 2003-651916	20030829 <--
EP 1522313	A1	20050413	EP 2004-26577	19991222 <--
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WO 2005037259	A2	20050428	WO 2004-US27574	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:		
US 1998-113786P	P	19981223 <--
US 1999-470951	B2	19991222 <--
US 1999-385214	A	19990827 <--
EP 1999-968939	A3	19991222 <--
US 2003-651916	A	20030829

AB The present invention relates to a novel method of preventing and/or treating neoplasia disorders in a subject that is in need of such prevention or treatment by administering to the subject at least one COX-2 inhibitor in combination with an EGF **receptor** antagonist. Compns., pharmaceutical compns. and kits are also described.

L24 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:513328 HCAPLUS
DOCUMENT NUMBER: 141:71561
TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors
INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.;

Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin, John J.; Li, Ge; Huang, Chia-yu; James, Ray A.; Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 731 pp., Cont.-in-part of U.S. Ser. No. 85,896.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2004122018	A1	20040624	US 2002-325896	20021219	<--
US 2002198216	A1	20021226	US 2001-940811	20010828	<--
US 2003229099	A1	20031211	US 2002-85896	20020227	<--
US 2004122018	A1	20040624	US 2002-325896	20021219	<--
US 2004122018	A1	20040624	US 2002-325896	20021219	<--
CA 2477328	AA	20030904	CA 2003-2477328	20030225	
WO 2003072549	A1	20030904	WO 2003-US5479	20030225	
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
BR 2003008071	A	20041221	BR 2003-8071	20030225	
EP 1492772	A1	20050105	EP 2003-711214	20030225	
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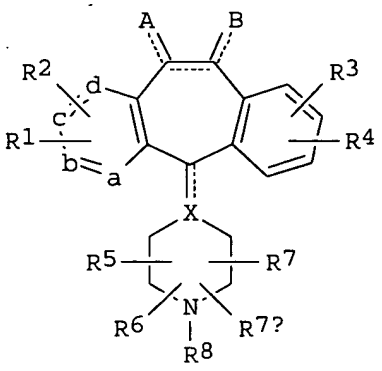
PRIORITY APPLN. INFO.:

US 2001-940811	A2	20010828	<--
US 2002-85896	A2	20020227	
US 2000-229183P	P	20000830	<--
US 2002-325896	A	20021219	
WO 2003-US5479	W	20030225	

OTHER SOURCE(S): MARPAT 141:71561

GI



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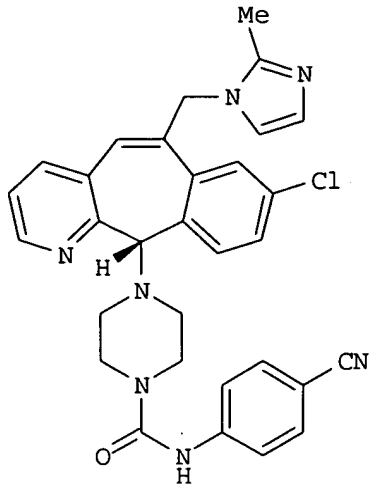

II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

L24 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:100803 HCAPLUS
DOCUMENT NUMBER: 140:139483
TITLE: Method for enhancing the effectiveness of therapies of hyperproliferative diseases
INVENTOR(S): Chang, Yan; Sasak, Vodek
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 176,235.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004023925	A1	20040205	US 2003-408723	20030407 <--
US 2003013681	A1	20030116	US 2002-176235	20020620 <--
US 6680306	B2	20040120		
CN 1543351	A	20041103	CN 2002-816003	20020621 <--
US 2004043962	A1	20040304	US 2003-657383	20030908 <--
WO 2004091634	A1	20041028	WO 2004-US10675	20040407

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 2001-299991P	P	20010621 <--
	US 2002-176235	A2	20020620
	US 2003-408723	A	20030407
	US 2003-461006P	P	20030407
	US 2003-474562P	P	20030530

AB The efficacy of conventional cancer therapies such as surgery, chemotherapy and **radiation** is enhanced by the use of a therapeutic material which binds to and interacts with galectins. The therapeutic material can enhance apoptosis thereby increasing the effectiveness of oncolytic agents. It can also inhibit angiogenesis thereby moderating tumor growth and/or metastasis.

L24 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:971730 HCAPLUS
DOCUMENT NUMBER:	140:27844
TITLE:	Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors
INVENTOR(S):	Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin, John J.; Li, Ge; Huang, Chia-Yu; James, Ray A.; Bishop, W. Robert; Wang, James J. S.; Desai, Jagdish A.
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 519 pp., Cont.-in-part of U.S. Pat. Appl. 2002 198,216. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003229099	A1	20031211	US 2002-85896	20020227 <--
US 2002198216	A1	20021226	US 2001-940811	20010828 <--
US 2004122018	A1	20040624	US 2002-325896	20021219 <--

US 2004122018	A1	20040624	US 2002-325896	20021219 <--
US 2004122018	A1	20040624	US 2002-325896	20021219 <--
CA 2477328	AA	20030904	CA 2003-2477328	20030225
WO 2003072549	A1	20030904	WO 2003-US5479	20030225

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

BR 2003008071	A	20041221	BR 2003-8071	20030225
EP 1492772	A1	20050105	EP 2003-711214	20030225

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:	US 2000-229183P	P	20000830 <--
	US 2001-940811	A2	20010828 <--
	US 2002-85896	A2	20020227
	US 2002-325896	A	20021219
	WO 2003-US5479	W	20030225

OTHER SOURCE(S): MARPAT 140:27844
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; one of a, b, d, e = N, N:O; remaining a, b, d, e = C (wherein each C atom has an R1 or R2 bound to said carbon); or each a, b, d, e = C (wherein each C atom has an R1 or R2); R1-R4 = H, halo, CF3, alkoxy, etc.; R5-R7, R9 = H, CF3, alkyl, aryl, etc.; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; dotted line = single or double bond; X = N, CH; A, B = (un)substituted CH, CH2], their stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs which are useful for inhibiting farnesyl protein transferase, were prepared E.g., a multi-step synthesis of II, was given. The compds. I have an FTP IC50 in the range of 0.05 nM to 100 nM. Also disclosed are pharmaceutical compns. comprising title compds. I as well as methods of using them to treat proliferative diseases such as cancer.

L24 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472516 HCAPLUS
DOCUMENT NUMBER: 139:53031
TITLE: Preparation of furopyrimidinones as mitotic kinesin inhibitors for treatment of cancer
INVENTOR(S): Fraley, Mark E.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003050122 A2 20030619 WO 2002-US38487 20021202 <--
WO 2003050122 A3 20031204
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2467726 AA 20030619 CA 2002-2467726 20021202 <--
EP 1465896 A2 20041013 EP 2002-799202 20021202 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
JP 2005515208 T2 20050526 JP 2003-551146 20021202 <--
US 2005032817 A1 20050210 US 2004-497382 20040601 <--
PRIORITY APPLN. INFO.: US 2001-338380P P 20011206 <--
WO 2002-US38487 W 20021202
OTHER SOURCE(S): MARPAT 139:53031
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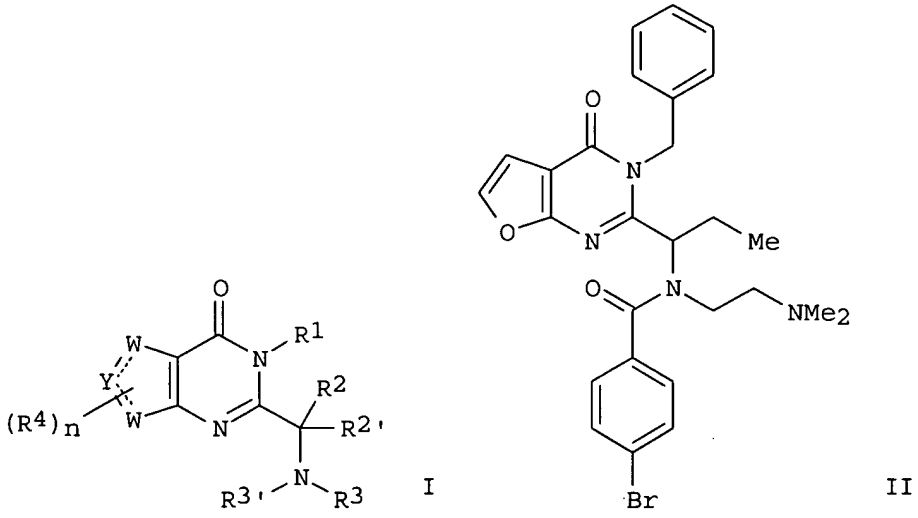

AB Syntheses for title compds. I [wherein one of W, Y, or Z = O and the other 2 = CH; R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, aralkyl, or heterocyclyl; R2, R2', R3, and R3' = independently H, CO2H, perfluoroalkyl, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)alkyl; or CR3R3' = (un)substituted heteroalkyl; R4 = halo, OH, CN, CO2H, perfluoroalkyl(oxy), SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, CO-Ob-(cyclo)alkyl, CO-Ob-alkenyl, CO-Ob-alkynyl,

CO-Ob-aryl, or CO-Ob-heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; n = 0-2; and pharmaceutically acceptable salts or stereoisomers thereof] as KSP kinesin inhibitors are given (no data). For example, a detailed synthesis for the preparation of II is outlined. The scheme involves the reaction of tert-Bu 2-furylcarbamate with CO2 and benzylamine in the presence of t-BuLi, substitution with butyryl chloride, cyclization, bromination, addition of N,N-dimethylethylenediamine, and coupling with 4-bromobenzoyl chloride. I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases associated with KSP kinesin activity, such as cancer (no data).

L24 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472471 HCAPLUS
DOCUMENT NUMBER: 139:69276
TITLE: Preparation of thienopyrimidines as mitotic kinesin inhibitors for the treatment of cancer
INVENTOR(S): Fraley, Mark E.; Hartman, George D.; Hoffman, William F.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2003050064	A2	20030619	WO 2002-US38417		20021202	<--
WO 2003050064	A3	20031016				
WO 2003050064	B1	20031218				
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CA 2467722	AA	20030619	CA 2002-2467722		20021202	<--
EP 1463733	A2	20041006	EP 2002-804714		20021202	<--
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JP 2005516007	T2	20050602	JP 2003-551092		20021202	<--
PRIORITY APPLN. INFO.:			US 2001-338383P	P	20011206	<--
			WO 2002-US38417	W	20021202	

OTHER SOURCE(S): MARPAT 139:69276
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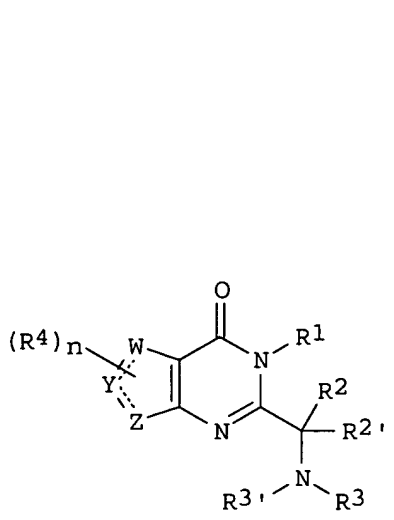

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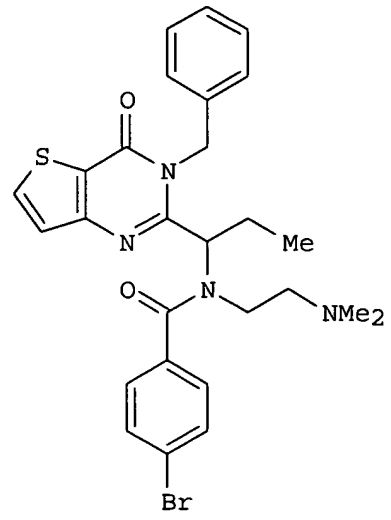

II

AB Title compds. I [wherein one of W, Y, or Z = S and the other 2 = CH; R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, aralkyl, or heterocyclyl; R2, R2', R3, and R3' = independently H, CO2H, perfluoroalkyl, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)alkyl; or CR3R3' = (un)substituted heteroalkyl; R4 = halo, OH, CN, CO2H, perfluoroalkyl(oxy), SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, CO-Ob-(cyclo)alkyl, CO-Ob-alkenyl, CO-Ob-alkynyl, CO-Ob-aryl, or CO-Ob-heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; n = 0-2; and pharmaceutically acceptable salts or stereoisomers thereof] were prepared for inhibiting KSP kinesin. For example, amidation of Me 3-aminothiophene-2-carboxylate with butyryl chloride afforded Me 3-(butyrylamino)thiophene-2-carboxylate, which was saponified to give the acid. Amidation with benzylamine, followed by cyclization provided 3-benzyl-2-propylthieno[3,2-d]pyrimidin-4(3H)-one. Bromination, coupling with N,N-dimethylethylenediamine, and reaction with 4-bromobenzoyl chloride gave the N-[1-(thienopyrimidinyl)propyl]benzamide II. The latter inhibited human poly-histidine tagged KSP motor domain with an IC50 value of ≤50 μM. Thus, I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases associated with KSP kinesin activity, such as cancer (no data). Preparation of thienopyrimidine kinesin inhibitors from thiophenes, amines, and acid chlorides.

L24 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472337 HCAPLUS
DOCUMENT NUMBER: 139:69275
TITLE: Preparation of thiazolopyrimidinones as mitotic kinesin inhibitors for treatment of cancer
INVENTOR(S): Fraley, Mark E.; Hartman, George D.; Hoffman, William F.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049679	A2	20030619	WO 2002-US38313	20021202 <--
WO 2003049679	A3	20041007		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1481077	A2	20041201	EP 2002-786830	20021202 <--
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JP 2005520793	T2	20050714	JP 2003-550730	20021202 <--
US 2005171122	A1	20050804	US 2003-497414	20021202 <--
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			WO 2002-US38313 W	20021202

OTHER SOURCE(S): MARPAT 139:69275
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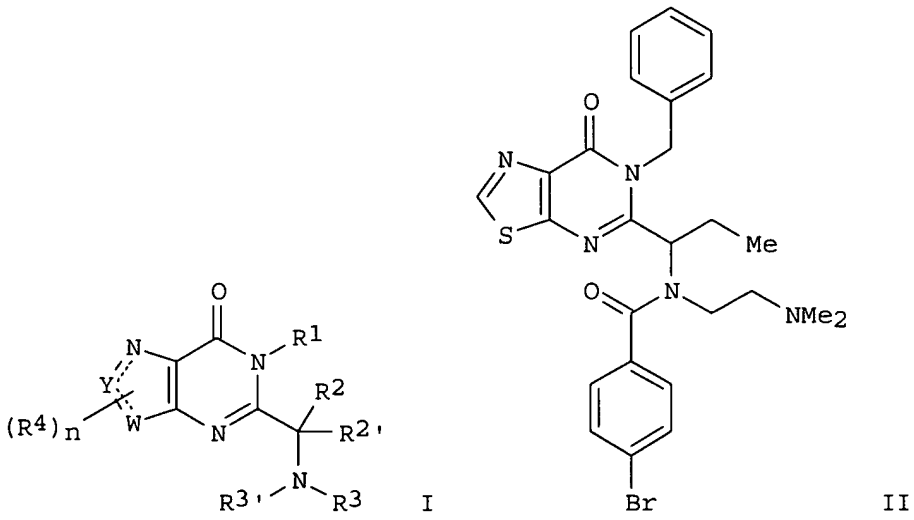


AB Syntheses for title azolopyrimidinone compds. I [wherein Y = CH or N; W = CH, S, or O; R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aralkyl, aryl, or heterocyclyl; R2, R2', R3, and R3' = independently H, perfluoroalkyl, CO2H, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl,

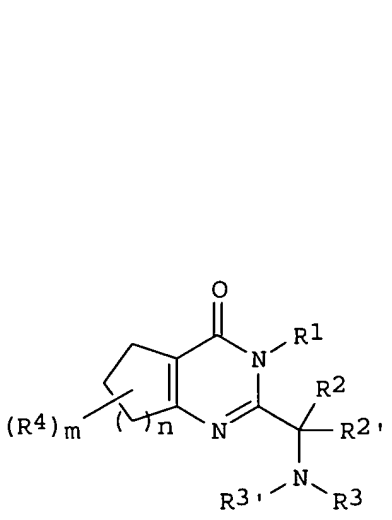
(CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)cyclyl; or NR3R3' = (un)substituted heterocyclyl; R4 = independently halo, OH, CN, perfluoroalkyl(oxy), CO2H, (CO)aNR7R8, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted CO-Ob-(cyclo)alkyl, CO-Ob-aryl, CO-Ob-heterocyclyl, (cyclo)alkyl, alkenyl, alkynyl, aryl, or heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl, aryl, or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; n = 0-2; and pharmaceutically acceptable salts or stereoisomers thereof] as KSP kinesin inhibitors are given (no data). For example, a detailed synthesis for the preparation of II is outlined (no data). The reaction scheme involves the cyclization of Et 5-amino-1,3-thiazole-4-carboxylate with tri-Me orthobutyrate and benzylamine to afford the [1,3]thiazolo[5,4-d]pyrimidin-7(6H)-one intermediate, followed by bromination, amination with N,N-dimethylethylenediamine, and amidation with 4-bromobenzoyl chloride. I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases associated with KSP kinesin activity, such as cancer (no data).

L24 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:472336 HCAPLUS
DOCUMENT NUMBER: 139:53029
TITLE: Preparation of cyclopenta[d]pyrimidinones as mitotic kinesin inhibitors for the treatment of cancer
INVENTOR(S): Fraley, Mark E.; Garbaccio, Robert M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049678	A2	20030619	WO 2002-US38312	20021202 <--
WO 2003049678	A3	20050519		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2468266	AA	20030619	CA 2002-2468266	20021202 <--
US 2005107404	A1	20050519	US 2003-497413	20021202 <--
EP 1551812	A2	20050713	EP 2002-804712	20021202 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-338379P P 20011206 <--
WO 2002-US38312 W 20021202

OTHER SOURCE(S): MARPAT 139:53029
GI



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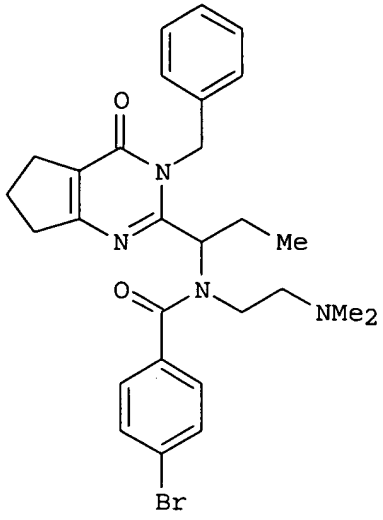

II

AB Title compds. I [wherein one of R1 = H, perfluoroalkyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, aralkyl, or heterocyclyl; R2, R2', R3, and R3' = independently H, CO2H, perfluoroalkyl, SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; or CR2R2' = (un)substituted (hetero)alkyl; or CR3R3' = (un)substituted heteroalkyl; R4 = halo, OH, CN, CO2H, perfluoroalkyl(oxy), SO2NR7R8, or (un)substituted (CO)aOb-(cyclo)alkyl, (CO)aOb-alkenyl, (CO)aOb-alkynyl, (CO)aOb-aryl, (CO)aOb-heterocyclyl, or SO2-alkyl; R7 and R8 = independently H, SO2Ra, CON(Rb)2, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, CO-Ob-(cyclo)alkyl, CO-Ob-alkenyl, CO-Ob-alkynyl, CO-Ob-aryl, or CO-Ob-heterocyclyl; or NR7R8 = (un)substituted heterocyclyl; Ra = (cyclo)alkyl or heterocyclyl; Rb = H, (cyclo)alkyl, aryl, heterocyclyl, CO2-alkyl, CO-alkyl, or SO2Ra; a and b = independently 0-1; m = 0-3; n = 1-3; and pharmaceutically acceptable salts or stereoisomers thereof] were prepared for inhibiting KSP kinesin. For example, reaction of Et 2-aminocyclopentenecarboxylate with 1,1,1-trimethoxybutane and benzylamine gave 3-benzyl-2-propyl-3,5,6,7-tetrahydro-4H-cyclopenta[d]pyrimidin-4-one. Bromination, substitution with N,N-dimethylethylenediamine, and coupling with 4-bromobenzoyl chloride provided II. The latter inhibited human poly-histidine tagged KSP motor domain with an IC50 value of ≤50 μM. Thus, I and pharmaceutical compns. thereof are useful for treating cellular proliferative diseases associated with KSP kinesin activity, such as cancer.

L24 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:472306 HCAPLUS
DOCUMENT NUMBER:	139:47130
TITLE:	Azolopyrimidinone compound mitotic kinesin inhibitors for the treatment of proliferative diseases
INVENTOR(S):	Fraley, Mark E.; Hartman, George D.; Hoffman, William F.
PATENT ASSIGNEE(S):	Merck & Co., Inc., USA
SOURCE:	PCT Int. Appl., 153 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049527	A2	20030619	WO 2002-US38488	20021202 <--
WO 2003049527	A3	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2467916	AA	20030619	CA 2002-2467916	20021202 <--
EP 1458726	A2	20040922	EP 2002-798478	20021202 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

JP 2005516000	T2	20050602	JP 2003-550582	20021202 <--
US 2005176737	A1	20050811	US 2003-497385	20021202 <--
PRIORITY APPLN. INFO.:			US 2001-338779P P	20011206 <--
			WO 2002-US38488 W	20021202

OTHER SOURCE(S): MARPAT 139:47130

AB The invention provides azolopyrimidinone compds. that are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention also provides compns. which comprise these compds., and methods of using them to treat cancer in mammals. Preparation of N-[1-(5-benzyl-3-bromo-4-oxo-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimidin-6-yl)propyl]-4-bromo-N-[2-(dimethylamino)ethyl]benzamide is described.

L24 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:377149 HCAPLUS
DOCUMENT NUMBER: 138:362662
TITLE: EGF **receptor**-mediated signal modulation-based method for prediction or prognosis of the efficacy of a tumor treatment
INVENTOR(S): Waldenmaier, Dirk; Metzger, Rainer; Kischkel, Frank
PATENT ASSIGNEE(S): Cellcontrol Biomedical Laboratories AG, Germany
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040724	A1	20030515	WO 2002-EP12392	20021106 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10154540 A1 20030522 DE 2001-10154540 20011107
PRIORITY APPLN. INFO.: DE 2001-10154540 A 20011107 <--

AB A method for prediction or prognosis of the efficacy of a tumor treatment is disclosed, comprising an interaction partner and a therapeutic agent, the efficacy of which is predicted or prognosed by measuring a modulation of an EGF **receptor**-mediated signal. The invention further provides a method for identification and modification of interaction partners and therapeutic agents for tumor treatment.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:376563 HCAPLUS
DOCUMENT NUMBER: 138:385439
TITLE: Preparation of quinazolinone mitotic kinesin inhibitors for treating cancer
INVENTOR(S): Fraley, Mark E.; Hoffman, William F.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039460	A2	20030515	WO 2002-US35111	20021101 <--
WO 2003039460	A3	20030731		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2465491	AA	20030515	CA 2002-2465491	20021101 <--
EP 1444209	A2	20040811	EP 2002-799174	20021101 <--

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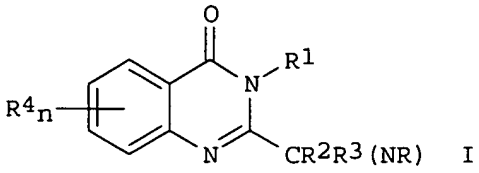
JP 2005511581	T2	20050428	JP 2003-541752	20021101 <--
US 2004259826	A1	20041223	US 2004-494899	20040507 <--

PRIORITY APPLN. INFO.: US 2001-344453P P 20011107 <--
WO 2002-US35111 W 20021101

OTHER SOURCE(S): MARPAT 138:385439
GI



I

AB The present invention relates to quinazolinones (shown as I; variables defined below; e.g. 3-benzyl-2-[1-(4-methylpiperazin-1-yl)propyl]quinazolin-4(3H)-one) that are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention also related to compns. which comprise these compds., and methods of using them to treat cancer in mammals. Twelve examples of I were found in a kinesin ATPase in vitro assay to have IC50 ≤50 μM. Although the methods of preparation are not claimed, 1 example preparation of I and characterization data for another 10 examples of I are included. For I: NR = 5-12 membered N-containing heterocycle, which is optionally substituted with 1-6 R5 groups and which optionally incorporates 1-2 addnl. heteroatoms = N, O and S in the heterocycle; a = 0, 1; b = 0, 1; m = 0-2; n = 0-4; R1 = H, C1-C10 alkyl, aryl, C2-C10 alkenyl, C2-C10 alkynyl, C1-C6 perfluoroalkyl, C3-C8 cycloalkyl, and heterocyclyl. R2 and R3 = H, (C:O)aObC1-C10 alkyl, (C:O)aObaryl, (C:O)aObC2-C10 alkenyl, (C:O)aObC2-C10 alkynyl, CO2H, C1-C6 perfluoroalkyl, (C:O)aObC3-C8 cycloalkyl, (C:O)aObheterocyclyl, SO2NR7R8, and SO2C1-C10 alkyl; R4 = (C:O)aObC1-C10 alkyl, (C:O)aObaryl, (C:O)aObC2-C10 alkenyl, (C:O)aObC2-C10 alkynyl, CO2H, halo, OH, ObC1-C6 perfluoroalkyl, (C:O)aNR7R8, CN, (C:O)aObC3-C8 cycloalkyl, (C:O)aObheterocyclyl, SO2NR7R8, and SO2C1-C10 alkyl; R5 is (C:O)aObC1-C10 alkyl, (C:O)aObaryl, C2-C10 alkenyl, C2-C10 alkynyl, (C:O)aOb heterocyclyl, CO2H, halo, CN, OH, ObC1-C6 perfluoroalkyl, Oa(C:O)bNR7R8, oxo, CHO, N(O)R7R8, or C(O)aObC3-C8 cycloalkyl; addnl. details are given in the claims.

L24 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:219666 HCAPLUS
DOCUMENT NUMBER: 138:231716
TITLE: Valproic acid and derivatives thereof for the combination therapy of human cancers, for the treatment of tumor metastasis and minimal residual disease
INVENTOR(S): Heinzel, Thorsten; Gottlicher, Martin; Hentsch, Bernd; Wels, Winfried Stephan; Pelicci, Pier Giuseppe; Minucci, Saverio; Herrlich, Peter A.; Groner, Bernd
PATENT ASSIGNEE(S): G2M Cancer Drugs AG, Germany
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1293205	A1	20030319	EP 2001-121722	20010918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

CA 2460713	AA	20030327	CA 2002-2460713	20020917 <--
WO 2003024442	A2	20030327	WO 2002-EP10419	20020917 <--
WO 2003024442	A3	20030918		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1427403	A2	20040616	EP 2002-777129	20020917 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

EP 1529527	A2	20050511	EP 2005-101081	20020917 <--
EP 1529527	A3	20050525		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK

JP 2005512961	T2	20050512	JP 2003-528538	20020917 <--
US 2005038113	A1	20050217	US 2004-489770	20041029 <--
PRIORITY APPLN. INFO.:			EP 2001-121722 A	20010918 <--
			EP 2002-777129 A3	20020917
			WO 2002-EP10419 W	20020917

OTHER SOURCE(S): MARPAT 138:231716

AB The invention discloses the use of valproic acid and derivs. thereof as inhibitors of enzymes having histone deacetylase activity for the therapeutic treatment of human cancers in combination with established therapeutic principles. The invention also discloses the use of these compds. for the treatment of tumor metastasis and minimal residual disease. The invention includes the manufacture of a clin. used substance for the treatment of human cancers.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:202621 HCAPLUS
DOCUMENT NUMBER: 138:238027
TITLE: Preparation of 3-(2-indolyl)quinolin-2(1H)-ones as tyrosine kinase inhibitors
INVENTOR(S): Peckham, Jennifer P.; Hoffman, William F.; Arrington, Kenneth L.; Fraley, Mark E.; Hartman, George D.; Kim, Yuntae; Hanney, Barbara; Spencer, Keith L.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020699	A2	20030313	WO 2002-US27114	20020826 <--
WO 2003020699	A3	20030522		

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LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004235826 A1 20041125 US 2004-487589 20040224 <--
PRIORITY APPLN. INFO.: US 2001-316123P P 20010830 <--
WO 2002-US27114 W 20020826

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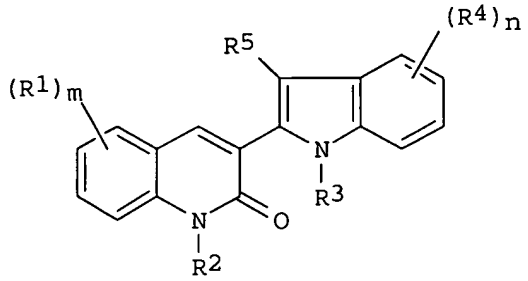

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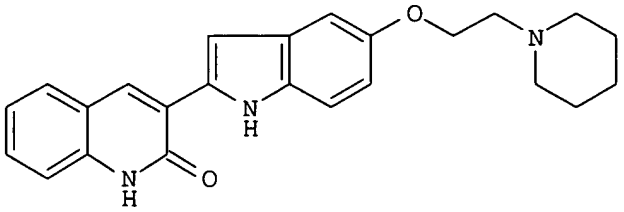


II

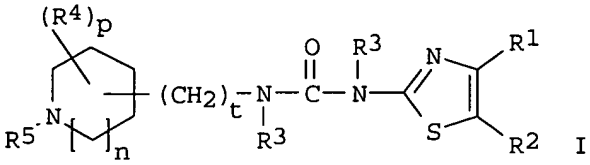
AB Title compds., including I (R groups undefined), were prepared and inhibitors, regulators, and/or modulators of tyrosine kinase signal transduction. For example, 1-(tert-butoxycarbonyl)-5-[(tert-butyldimethylsilyl)oxy]-1H-indol-2-ylboronic acid was coupled with 2-chloro-3-iodoquinoline (preparation of starting materials given) in the presence of Pd(PPh3)4 and K3PO4 in dioxane to give the protected 3-(2-indolyl)quinoline derivative Deprotection using triethylamine trihydrofluoride afforded the alc. Reaction with 1-(2-chloroethyl)piperidine•HCl and Cs2CO3 in DMF followed by reflux at 110° in AcOH and H2O for 12 h provided II. Compds.. of the invention inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01 μM - 5.0 μM. Thus, I and compns. containing I are useful for the treatment of tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

L24 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:154204 HCAPLUS
DOCUMENT NUMBER: 138:165738
TITLE: Tyrosine kinase inhibitors and their use in disease treatment

INVENTOR(S): Hartman, George D.; Tucker, Thomas J.; Sisko, John T.; Smith, Anthony M.; Lumma, William C., Jr.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015717	A2	20030227	WO 2002-US27149	20020813 <--
WO 2003015717	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004242637	A1	20041202	US 2004-487166	20040217 <--
PRIORITY APPLN. INFO.:			US 2001-313374P P	20010817 <--
			WO 2002-US27149 W	20020813

OTHER SOURCE(S): MARPAT 138:165738
GI



I

AB The present invention relates to compds. I (n = 1,2,3; p,t = 1,2; R1 = H, halo, C1-8-alkyl; R2 = Ph, CN, C(:O)NRaRb, halo, C3-6-cycloalkyl, C.tplbond.CRc; R4 = H, halo, OH, C1-8-alkyl, C1-8-alkoxy; R5 = H, Ph, C1-8-alkyl, CO2Rd, C(:O)Rd, SO2Rd; Ra,Rb = H, Ph, C1-8-alkyl, CO2Rd, C(:O)Rd, SO2Rd; Rc = H, Ph, C1-8-alkyl; Rd = Ph, C1-8-alkyl, benzyl) which inhibit, regulate and/or modulate tyrosine kinase signal transduction. I may be used to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals. Thus, compds. such as N-(5-phenylthiazol-2-yl)-N'-(4-aminopiperidin-4-yl)urea were prepared and tested for effects on VEGF **receptor** kinase, FLT-1 kinase, and HUVEC mitogenesis. I compds. inhibited HUVEC mitogenesis with IC50 values of 0.01-5.0 μM.

L24 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:117808 HCAPLUS
DOCUMENT NUMBER: 138:170248
TITLE: Preparation of 4-(thiazolyl)-2-pyrimidinamines as tyrosine kinase inhibitors

INVENTOR(S): Fraley, Mark E.; Hoffman, William F.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011838	A1	20030213	WO 2002-US23882	20020727 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004181066	A1	20040916	US 2004-485291	20040129 <--
PRIORITY APPLN. INFO.:			US 2001-309407P P	20010801 <--
			WO 2002-US23882 W	20020727

OTHER SOURCE(S): MARPAT 138:170248
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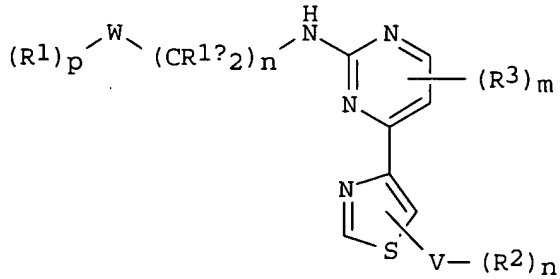

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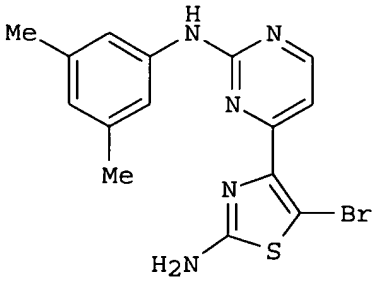


II

AB The present invention relates to title compds. I [wherein R1a = H, (un)substituted alkyl, OR8, or N(R8)2; R1 and R2 = independently H, halo, CF3, (CH2)tR9COR8, COR9, (CH2)tOR8, CN, (CH2)tNR7R8, (CH2)CONR7R8, CO2R8,

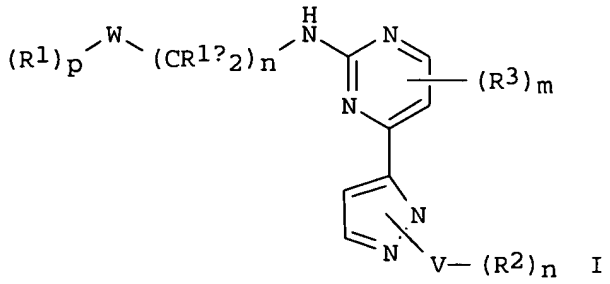
(CH2)tSO0-2(CH2)tNR7R8, or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkenyl, or alkynyl; R3 = H, CN, halo, N(R8)2, OR8, or (un)substituted (ar)alkyl or aryl; R7 = H or (un)substituted (ar)alkyl; R8 = independently H or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or aralkyl; or NR7R8 = (un)substituted heterocyclyl; R9 = independently (un)substituted alkyl, heterocyclyl, or aryl; W = aryl or heterocyclyl; m = 0-2; n = independently 0-6; p = 0-4; t = independently 0-6; or pharmaceutically acceptable salts, hydrates, or stereoisomers thereof], which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions. For example, cyclization of 2-bromo-1-[2-(methylthio)pyrimidin-4-yl]ethanone (3-step preparation given) with thiourea in EtOH gave 5-bromo-4-[2-(methylthio)pyrimidin-4-yl]-1,3-thiazol-2-amine•HBr. Oxidation to the methylsulfinyl derivative using oxone followed by substitution with 3,5-dimethylaniline afforded II. In bioassays, I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC values between 0.01 M and 5.0 M. Thus, I are useful for the treatment of angiogenesis, cancer, tumor growth, atherosclerosis, age relate80d macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:117807 HCAPLUS
DOCUMENT NUMBER: 138:153548
TITLE: Preparation of 4-(pyrazolyl)-2-pyrimidinamines as tyrosine kinase inhibitors
INVENTOR(S): Fraley, Mark E.; Peckham, Jennifer P.; Arrington, Kenneth L.; Hoffman, William F.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003011837	A1	20030213	WO 2002-US23879		20020726 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004235875	A1	20041125	US 2004-485296		20040129 <--
PRIORITY APPLN. INFO.:			US 2001-309399P	P	20010801 <--
			WO 2002-US23879	W	20020726

OTHER SOURCE(S): MARPAT 138:153548
GI



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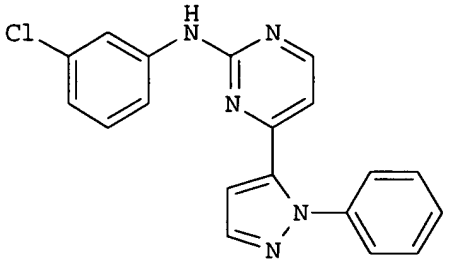

II

AB The present invention relates to title compds. I [wherein R1a = H, (un)substituted alkyl, OR8, or N(R8)2; R1 and R2 = independently H, halo, CF3, (CH2)tR9COR8, COR9, (CH2)tOR8, CN, (CH2)tNR7R8, (CH2)tCONR7R8, CO2R8, (CH2)tSO0-2(CH2)tNR7R8, or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkenyl, or alkynyl; R3 = independently H, CN, halo, N(R3)2, (CH2)tOR8, or (un)substituted (ar)alkyl or aryl; R7 = independently H or (un)substituted (ar)alkyl; R8 = independently H or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or aralkyl; or NR7R8 = (un)substituted heterocyclyl; R9 = independently (un)substituted heterocyclyl, alkyl, or aryl; V = a bond, aryl, or heterocyclyl; W = aryl or heterocyclyl; m = 0-2; n = 0-6; p = 0-4; t = independently 0-6; and pharmaceutically acceptable salts, hydrates, and stereoisomers thereof], which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions. For example, 2-(methylthio)pyrimidine-4-carboxylic acid was amidated with dimethylhydroxylamine•HCl in the presence of EDC and TEA, and the product treated with MeMgBr in Et2O to give 1-[2-(methylthio)pyrimidin-4-yl]ethanone. Coupling with N,N-dimethylformamide dimethylacetal followed by cyclization with phenylhydrazine afforded 2-(methylthio)-4-(1-phenyl-1H-pyrazol-3/5-yl)pyrimidine. Oxidation with oxone and reaction with 3-chloroaniline provided the 4-(pyrazolyl)-2-pyrimidinamine II. In bioassays, I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01 μM and 5.0 μM. Thus, I are useful for the treatment of angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:117806 HCAPLUS
DOCUMENT NUMBER: 138:153547
TITLE: Preparation of 4-(imidazolyl)-2-pyrimidinamines as tyrosine kinase inhibitors
INVENTOR(S): Bilodeau, Mark T.; Manley, Peter J.; Balitza,

Adrienne; Rodman, Leonard; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011836	A1	20030213	WO 2002-US23764	20020726 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004220201	A1	20041104	US 2004-485170	20040129 <--
PRIORITY APPLN. INFO.:			US 2001-309400P P	20010801 <--
			WO 2002-US23764 W	20020726

OTHER SOURCE(S): MARPAT 138:153547
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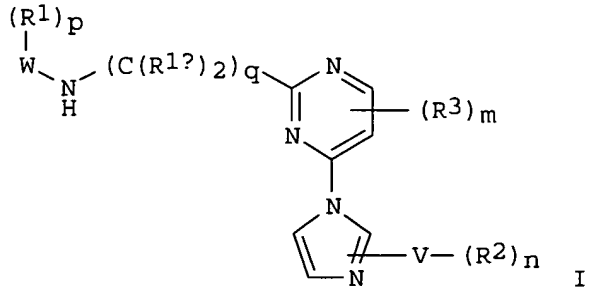

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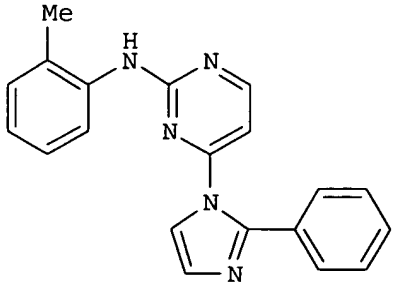

II

AB The present invention relates to title compds. I [wherein R1a = H, (un)substituted alkyl, or OR8, or N(R8)2; R1 and R2 = independently H, halo, CF3, (CH2)tR9COR8, COR9, (CH2)tOR8, CN, (CH2)tNR7R8, (CH2)tCONR7R8, CO2R8, (CH2)tSOq(CH2)tNR7R8, oxido, or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkenyl, or alkynyl; R3 = H, CN, halo, N(R8)2, (CH2)tOR8, or

(un)substituted (ar)alkyl or aryl; R7 = independently H or (un)substituted (ar)alkyl; R8 = independently H or (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or aralkyl; or NR7R8 = (un)substituted heterocyclyl; R9 = independently (un)substituted heterocyclyl, alkyl, or aryl; V = bond, aryl, or heterocyclyl; W = aryl or heterocyclyl; m = 0-3; n = 0-6; p = 0-4; q = undefined; t = 0-6; or pharmaceutically acceptable salts, hydrates or stereoisomers thereof], which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions. For example, 2-phenylimidazole was coupled with 4-chloro-2-(methylthio)pyrimidine in the presence of NaH in DMF and the product oxidized using sodium tungstate dihydrate and H2O2 in EtOAc to give 2-(methylsulfonyl)-4-(2-phenyl-1H-imidazol-1-yl)pyrimidine. Substitution with 2-methylaniline and purification by reverse phase chromatog. afforded II•TFA. In bioassays, I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01 μM and 5.0 μM. Thus, I are useful for the treatment of angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:97306 HCAPLUS
DOCUMENT NUMBER: 138:137303
TITLE: Preparation of fused heterocycle substituted aminothiazolecarbonitriles as tyrosine kinase inhibitors
INVENTOR(S): Bilodeau, Mark T.; Manley, Peter J.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003009852	A1	20030206	WO 2002-US23191		20020719 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004235867	A1	20041125	US 2004-484986		20040123 <--
PRIORITY APPLN. INFO.:			US 2001-307443P	P	20010724 <--
			WO 2002-US23191	W	20020719

OTHER SOURCE(S): MARPAT 138:137303
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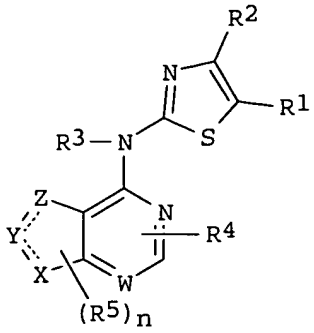

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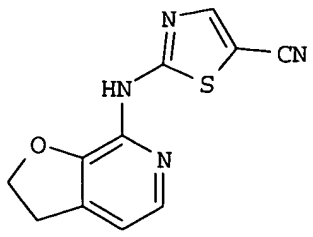

II

AB The present invention relates to the preparation of title compds. I [wherein X, Y, and Z = C, S, N, or O, provided that at least one of X, Y, or Z = C; W = C or N; n = 0-6; R1, R2, and R4 = independently H, perfluoroalkyl(oxy), OH, CN, halo, or (un)substituted (CO)rOs-alkyl, (CO)rOs-alkenyl, (CO)rOs-alkynyl, (CO)rOs-aryl, (CO)rOs-heterocyclyl, or alkyl-NRaRb; R3 = H, SO2Rc, (CO)rRc, or CO2Rc; R5 = R3 or Or(CO)sNRaRb, halo, OH, oxo, perfluoroalkyl(oxy), CHO, CO2H, CN, or (un)substituted (CO)rOs-aryl, (CO)rOs-heterocyclyl, or (CO)rOs-alkyl; r = 0-1; s = 0-1; Ra and Rb = independently H, SO2Rc, CO2Rc, or (un)substituted (CO)r-alkyl, (CO)r-heterocyclyl, or (CO)r-aryl; or NRaRb = (un)substituted monocyclic or bicyclic heterocycle; Rc = (un)substituted alkyl, aryl, benzyl, or heterocyclyl; or pharmaceutically acceptable salts or stereoisomers thereof], which inhibit, regulate, and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions. For example, 7-bromofuro[2,3-c]pyridine was converted to the amine using benzophenone imine, NaOBu-t, racemic BINAP, and Pd2(dba)3 in dry toluene and then hydrogenated with 10% Pd/C in AcOH to give 2,3-dihydrofuro[2,3-c]pyridin-7-amine. Addition of 2-chloro-5-cyanothiazole in the presence of NaH in THF afforded the (furopyridinylamino)thiazolecarbonitrile II. In bioassays, I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.001 μM and 5.0 μM. Thus, I are useful for the treatment of angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:977797 HCAPLUS
DOCUMENT NUMBER: 138:55974
TITLE: Preparation of 2-anilino-4-(indol-1-yl)pyrimidines as tyrosine kinase inhibitors
INVENTOR(S): Kim, Yuntae; Hanney, Barbara
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002102783 A1 20021227 WO 2002-US18907 20020614 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004171630 A1 20040902 US 2003-481370 20031219 <--
PRIORITY APPLN. INFO.: US 2001-299343P P 20010619 <--
WO 2002-US18907 W 20020614

OTHER SOURCE(S): MARPAT 138:55974

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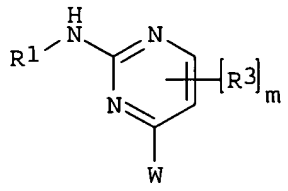
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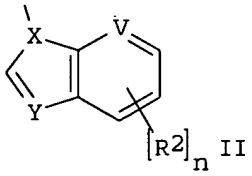
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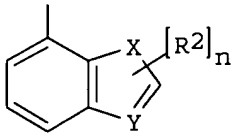
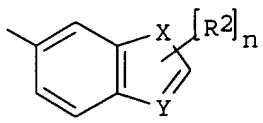

III


IV

AB The title compds. [I; W = II-IV; X, Y = C, N, provided that when X = N, then Y = C and when X = C, then Y = N; V = C, N; R1 = (un)substituted aryl, heterocyclyl; R2 = H, halo, alkyl, etc.; R3 = H, alkyl, aryl, etc.; m = 0-2; n = 0-5] which inhibit, regulate and/or modulate tyrosine kinase signal transduction, and therefore are useful in treating tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals, were prepared E.g., a multi-step synthesis of I [W = 4-fluoro-1H-indol-1-yl; R1 = Ph; R3 = H], starting from 2-thiouracil, was given.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:940624 HCAPLUS
DOCUMENT NUMBER: 138:248543
TITLE: Nucleic acid treatment of diseases or conditions related to levels of Ras, HER2 and HIV
INVENTOR(S): McSwiggen, James
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Incorporated, USA
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 211
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097114	A2	20021205	WO 2002-XA16840	20020529 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 9851819	A1	19980611	AU 1998-51819	19980112 <--
AU 729657	B2	20010208		
AU 9939188	A1	19990916	AU 1999-39188	19990713 <--
AU 769175	B2	20040115	AU 2000-56616	20000911 <--
WO 2002097114	A2	20021205	WO 2002-US16840	20020529 <--
WO 2002097114	A3	20030508		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2001-294140P	P 20010529 <--
			US 2001-296249P	P 20010606 <--
			US 2001-318471P	P 20010910 <--
			WO 2002-US16840	A 20020529
			AU 1995-26422	A3 19950518 <--
			US 1996-623891	A 19960325 <--
			AU 1996-76662	A3 19961025 <--

AB The present invention relates to nucleic acid mols., including enzymic nucleic acid mols., such as DNAzymes (e.g. DNA enzymes, catalytic DNA), siRNA, aptamers, and antisense that modulate the expression of Ras genes such as K-Ras, H-Ras, and/or N-Ras, HIV genes such as HIV-1, and HER2 (c-erbB2) gene. The sequence of human HER2 or Ras genes were screened for accessible sites using a computer-folding algorithm. Regions of the RNA that do not form secondary folding structure and contain potential enzymic nucleic acid mol. and/or antisense binding/cleavage sites are identified. The sequences of c-Ki-ras, c-Ha-ras, HER2, and HIV RNA binding/cleavage sites are provided, as are the sequences of designed enzymic nucleic acid mols., e.g., hammerhead ribozymes, DNAzymes, inozymes, zinzymes, and Amberzymes. [This abstract record is one of 2 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L24 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:927617 HCAPLUS
DOCUMENT NUMBER: 138:19530
TITLE: Nucleic acid treatment of diseases or conditions related to levels of Ras, HER2 and HIV
INVENTOR(S): McSwiggen, James

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Incorporated, USA
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 211
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097114	A2	20021205	WO 2002-US16840	20020529 <--
WO 2002097114	A3	20030508		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 9851819	A1	19980611	AU 1998-51819	19980112 <--
AU 729657	B2	20010208		
AU 9939188	A1	19990916	AU 1999-39188	19990713 <--
AU 769175	B2	20040115	AU 2000-56616	20000911 <--
WO 2002097114	A2	20021205	WO 2002-XA16840	20020529 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1390472	A2	20040225	EP 2002-734572	20020529 <--
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US 2003153521	A1	20030814	US 2002-238700	20020910 <--
WO 2003070912	A2	20030828	WO 2003-US5045	20030220 <--
WO 2003070912	A3	20041111		
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EP 1501853	A2	20050202	EP 2003-716093	20030220
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JP 2005517437	T2	20050616	JP 2003-569805	20030220
US 2005080031	A1	20050414	US 2003-724270	20031126 <--
US 2005176024	A1	20050811	US 2004-923354	20040820 <--
PRIORITY APPLN. INFO.:			US 2001-294140P P	20010529 <--

US 2001-296249P	P	20010606 <--
US 2001-318471P	P	20010910 <--
AU 1995-26422	A3	19950518 <--
US 1996-623891	A	19960325 <--
AU 1996-76662	A3	19961025 <--
US 2001-292217P	P	20010518 <--
US 2001-306883P	P	20010720 <--
US 2001-916466	A	20010725 <--
US 2001-311865P	P	20010813 <--
US 2002-358580P	P	20020220
US 2002-362016P	P	20020306
US 2002-363124P	P	20020311
WO 2002-US15876	A2	20020520
US 2002-157580	A2	20020529
WO 2002-US16840	A	20020529
US 2002-163552	A1	20020606
US 2002-386782P	P	20020606
US 2002-393924P	P	20020703
US 2002-406784P	P	20020829
US 2002-408378P	P	20020905
US 2002-409293P	P	20020909
US 2002-238700	A2	20020910
US 2002-251117	A1	20020919
US 2002-277494	A1	20021021
US 2003-440129P	P	20030115
WO 2003-US5028	A2	20030220
WO 2003-US5045	W	20030220
WO 2003-US5346	A2	20030220
US 2003-417012	B2	20030416
US 2003-422704	B2	20030424
US 2003-427160	A2	20030430
US 2003-444853	A2	20030523
US 2003-652791	A2	20030829
US 2003-693059	A2	20031023
US 2003-720448	A2	20031124
US 2003-724270	A2	20031126
US 2003-727780	A2	20031203
US 2004-757803	A2	20040114
US 2004-543480P	P	20040210
US 2004-780447	A2	20040213
US 2004-826966	A2	20040416
WO 2004-US13456	A2	20040430
WO 2004-US16390	A2	20040524

AB The present invention relates to nucleic acid mols., including enzymic nucleic acid mols., such as DNAzymes (e.g. DNA enzymes, catalytic DNA), siRNA, aptamers, and antisense that modulate the expression of Ras genes such as K-Ras, H-Ras, and/or N-Ras, HIV genes such as HIV-1, and HER2 (c-erbB2) gene. The sequence of human HER2 or Ras genes were screened for accessible sites using a computer-folding algorithm. Regions of the RNA that do not form secondary folding structure and contain potential enzymic nucleic acid mol. and/or antisense binding/cleavage sites are identified. The sequences of c-Ki-ras, c-Ha-ras, HER2, and HIV RNA binding/cleavage sites are provided, as are the sequences of designed enzymic nucleic acid mols., e.g., hammerhead ribozymes, DNAzymes, inozymes, zinzymes, and Amberzymes. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L24 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:889451 HCAPLUS
DOCUMENT NUMBER: 137:381947
TITLE: Methods and reagents for the rapid and efficient isolation of circulating cancer cells
INVENTOR(S): Terstappen, Leon W. M. M.; Rao, Galla Chandra; O'Hara, Shawn Mark; Liberti, Paul A.; Gross, Steven; Doyle, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 56 pp., Cont.-in-part of U.S. 6,365,362.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002172987	A1	20021121	US 2002-79939	20020219 <--
CA 2432361	AA	19990819	CA 1999-2432361	19990212 <--
CA 2432363	AA	19990819	CA 1999-2432363	19990212 <--
US 6365362	B1	20020402	US 1999-248388	19990212 <--
US 2002009759	A1	20020124	US 2001-904472	20010713 <--
US 6645731	B2	20031111		
CA 2438112	AA	20030807	CA 2002-2438112	20020219 <--
WO 2003065042	A1	20030807	WO 2002-US5233	20020219 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1360496	A1	20031112	EP 2002-806645	20020219 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005516217	T2	20050602	JP 2003-564585	20020219 <--
BR 2002007290	A	20050607	BR 2002-7290	20020219 <--
US 2003129676	A1	20030710	US 2002-269579	20021011 <--
JP 2005010177	A2	20050113	JP 2004-265687	20040913 <--

PRIORITY APPLN. INFO.:

US 1998-74535P	P	19980212 <--
US 1998-110202P	P	19981130 <--
US 1998-110279P	P	19981130 <--
US 1999-248388	A2	19990212 <--
US 2001-268859P	P	20010216 <--
US 2001-269270P	P	20010220 <--
US 2001-269271P	P	20010220 <--
CA 1999-2320418	A3	19990212 <--
JP 2000-531745	A3	19990212 <--
US 2001-904472	A1	20010713 <--
WO 2002-US5233	W	20020219

AB Methods and compns. are provided for detecting circulating tumor cells and assessing said cells for alterations in tumor-diathesis associated mols. Blood samples of women with stage III or metastatic breast cancer were reacted with anti-epithelial cell adhesion mol. monoclonal **antibodies** coupled to magnetic nanoparticles for immunomagnetic

separation of epithelial cells from the blood. The separated cells were further reacted with phycoerythrin conjugated with anti-cytokeratin monoclonal **antibody** to cytokeratin, peridinin chlorophyll protein-labeled anti-CD45, and cyanine 5-labeled anti-**HER-2**. The samples were analyzed by FACS. The number of circulating tumor cells was determined and shown to be useful in assessing tumor progression.

L24 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849467 HCAPLUS
DOCUMENT NUMBER: 137:346156
TITLE: Preventive/therapeutic method for cancer
INVENTOR(S): Naito, Kenichiro; Furuya, Shuichi; Tasaka, Akihiro; Ban, Toshikazu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2002087619	A1	20021107	WO 2002-JP4217		20020426	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
JP 2004002211	A2	20040108	JP 2002-127062		20020426	<--
US 2004138160	A1	20040715	US 2004-475990		20040302	<--
PRIORITY APPLN. INFO.:			JP 2001-131613	A	20010427	<--
			JP 2002-82019	A	20020322	
			WO 2002-JP4217	W	20020426	

AB A method of preventing/treating cancer characterized by blocking the information signal of a polymer belonging to the epithelial growth factor **receptor** family by selectively inhibiting ErbB-2 (HER2).
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849373 HCAPLUS
DOCUMENT NUMBER: 137:358081
TITLE: Diagnostic imaging compositions, their methods of synthesis, and use
INVENTOR(S): Li, Chun; Wen, Xiaoxia; Wu, Qing-Ping; Wallace, Sydney; Ellis, Lee M.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087498	A2	20021107	WO 2002-US12510	20020419 <--
WO 2002087498	A3	20031030		
WO 2002087498	C1	20031211		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2444483	AA	20021107	CA 2002-2444483	20020419 <--
US 2002197261	A1	20021226	US 2002-126369	20020419 <--
US 2003003048	A1	20030102	US 2002-126216	20020419 <--
EP 1389090	A2	20040218	EP 2002-766783	20020419 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:	US 2001-286453P	P	20010426 <--
	US 2001-334969P	P	20011204 <--
	US 2001-343147P	P	20011220
	WO 2002-US12510	W	20020419

AB Conjugate mols. comprising a ligand bonded to a polymer are disclosed. One such conjugate mol. comprises a ligand bonded to a polymer, a chelating agent bonded to the polymer, and a radioisotope chelated to the chelating agent. The conjugate mols. may be useful in detecting and/or treating tumors or biol. **receptors.** These conjugate mols. may be synthesized without the necessity of preactivation of the ligand using an SCN-polymer-chelating agent precursor. Conjugate mols. incorporating an annexin V ligand are particularly useful for visualizing apoptotic cells. Conjugate mols. incorporating a C225 ligand are particularly useful for targeting tumors expressing EGFR.

L24 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2002:777929 HCAPLUS
DOCUMENT NUMBER:	137:294954
TITLE:	Preparation of 2-(4-substituted-2-oxo-1,2-dihydropyridin-3-yl)-benzimidazoles as novel tyrosine kinase inhibitors
INVENTOR(S):	Wittman, Mark D.; Balasubramanian, Neelakantan; Velaparthi, Upender; Zimmermann, Kurt; Saulnier, Mark G.; Liu, Peiying; Sang, Xiaopeng; Frennesson, David B.; Stoffan, Karen M.; Tarrant, James G.
PATENT ASSIGNEE(S):	Bristol-Myers Squibb Company, USA
SOURCE:	PCT Int. Appl., 249 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079192	A1	20021010	WO 2002-US9402	20020326 <--
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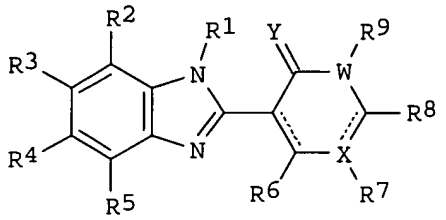
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2442428	AA	20021010	CA 2002-2442428	20020326 <--
EP 1381598	A1	20040121	EP 2002-723631	20020326 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300475	A	20040216	EE 2003-475	20020326 <--
CN 1514833	A	20040721	CN 2002-810516	20020326 <--
JP 2004534010	T2	20041111	JP 2002-577817	20020326 <--
BR 2002008373	A	20050222	BR 2002-8373	20020326 <--
ZA 2003007466	A	20050113	ZA 2003-7466	20030925 <--
NO 2003004308	A	20031126	NO 2003-4308	20030926 <--
BG 108206	A	20041130	BG 2003-108206	20030926 <--
PRIORITY APPLN. INFO.:			US 2001-279327P P	20010328 <--
			WO 2002-US9402 W	20020326

OTHER SOURCE(S): MARPAT 137:294954
GI



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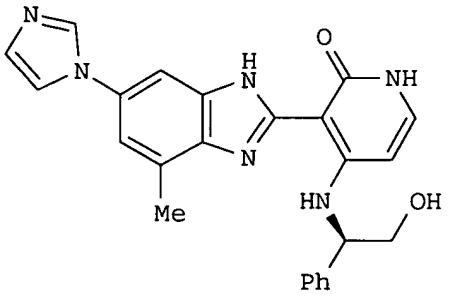

II

AB The title compds. [I; X = N, C, a bond, etc.; Y = O, S; W = N, C, O, S (if W = O or S, then R9 is absent); R1-R9 = H, alkyl, cycloalkyl, etc.] and their pharmaceutically acceptable salts which inhibit tyrosine kinase enzymes thereby making them useful as anti-cancer agents, were prepared Thus, reacting 3-[6-(imidazol-1-yl)-4-methyl-1H-benzimidazol-2-yl]-4-iodo-1H-pyridin-2-one (preparation given) with (S)-(-)-2-phenylglycinol in the presence of N-methylmorpholine in DMF afforded 52% (S)-II which showed IC50 of 1.0 μM in cytotoxicity assay (HT-29 human **colon**

tumor cell line). 30 Of the exemplified compds. I showed kinase activity of <25μM against one or more of the following kinases CDK, EMT, FAK, Her1, Her2, IGF, IR, LCK, MET, PDGF, VEGF. The compds. I are also useful for the treatment of other diseases which can be treated by inhibiting tyrosine kinase enzymes.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:637550 HCAPLUS
DOCUMENT NUMBER: 137:174955
TITLE: Targeted anti-tumor drug delivery systems
INVENTOR(S): Emanuel, David J.; Tendler, Craig L.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2002064168	A1	20020822	WO 2002-US4113		20020208	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
US 2002151508	A1	20021017	US 2002-67448		20020205	<--
CA 2437768	AA	20020822	CA 2002-2437768		20020208	<--
EP 1359942	A1	20031112	EP 2002-714873		20020208	<--
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JP 2004518717	T2	20040624	JP 2002-563960		20020208	<--
PRIORITY APPLN. INFO.:			US 2001-267807P	P	20010209	<--
			WO 2002-US4113	W	20020208	

AB Disclosed are methods for treating proliferative diseases, especially breast cancers, comprising administering (1) a therapeutically effective amount of a liposomal anthracycline composition in association with (2) a therapeutically effective amount of an **antibody** directed against the extracellular domain of a growth factor **receptor** and optionally in association with (3) a therapeutically effective amount of an addnl. antineoplastic agent. For example, the method comprises (1) administering PEGylated liposomal doxorubicin composition, followed by (2) cyclophosphamide, and (2) Trastuzumab (**antibody**).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:449450 HCAPLUS
DOCUMENT NUMBER: 137:706
TITLE: **Combination radiation** therapy and chemotherapy in conjunction with administration of growth factor **receptor antibody**

INVENTOR(S): Buchsbaum, Donald J.
PATENT ASSIGNEE(S): UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2002045653	A2	20020613	WO 2001-US46179		20011207	<--
WO 2002045653	A3	20030103				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
AU 2002039486	A5	20020618	AU 2002-39486		20011207	<--
US 2002076408	A1	20020620	US 2001-4833		20011207	<--
PRIORITY APPLN. INFO.:			US 2000-251787P	P	20001208	<--
			WO 2001-US46179	W	20011207	

AB The invention comprises a method of inhibiting tumor growth in tumors having growth factor **receptors** comprising administering, about simultaneously, **antibodies** to the target growth factor **receptors**, at least one chemotherapeutic agent, and **radiation** therapy.

L24 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:730715 HCAPLUS
DOCUMENT NUMBER: 135:288636
TITLE: Synergistic methods and compositions for treating cancer using two or more anticancer agents
INVENTOR(S): Lee, Francis Y.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2001072721	A2	20011004	WO 2001-US9193	20010322	<--
WO 2001072721	A3	20020613			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
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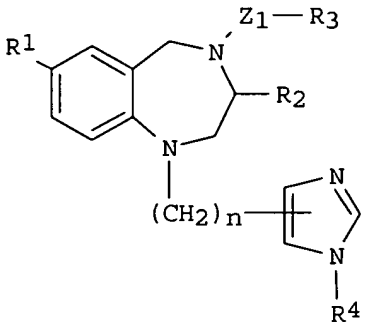
CA 2404712	AA	20011004	CA 2001-2404712		20010322 <--
EP 1272193	A2	20030108	EP 2001-920653		20010322 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003528864	T2	20030930	JP 2001-570634		20010322 <--
US 2002002162	A1	20020103	US 2001-817456		20010326 <--
US 6537988	B2	20030325			
NO 2002004610	A	20021125	NO 2002-4610		20020926 <--
ZA 2002007766	A	20030120	ZA 2002-7766		20020926 <--
PRIORITY APPLN. INFO.:			US 2000-192278P	P	20000327 <--
			WO 2001-US9193	W	20010322 <--

OTHER SOURCE(S): MARPAT 135:288636
GI



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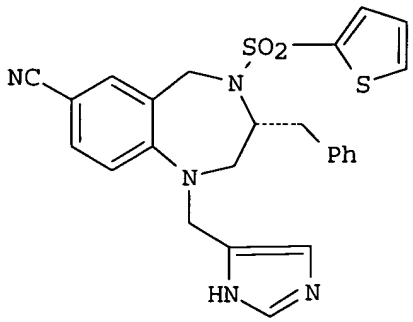

II

AB The present invention provides a synergistic method for the treatment of cancer which comprises administering a synergistically, therapeutically effective amount of: (i) at least agent selected from the group consisting of cytotoxic agents and cytostatic agents, and (ii) a compound of formula [I; R1 = Cl, Br, CN, substituted Ph, substituted pyridyl; R2 = alkyl, aralkyl; R3,R5 = substituted alkyl, aryl, heterocycle; R4 = H, alkyl; Z1 = CO, SO2, CO2, SO2N(R5); n = 1,2] or a pharmaceutically acceptable salt thereof. The present invention further provides a pharmaceutical composition for the synergistic treatment of cancer which comprises at least one agent selected from the group consisting of antiproliferative cytotoxic agents and antiproliferative cytostatic agents, a compound of formula I, and a pharmaceutically acceptable carrier. Synergism was observed when non-proliferating tumor cells were treated with diazepine II·HCl and **paclitaxel** (III) simultaneously or when III preceded II·HCl.

L24 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:167836 HCAPLUS
DOCUMENT NUMBER: 134:221445
TITLE: Dosages for treatment with anti-erbb2 **antibodies**
INVENTOR(S): Baughman, Sharon Ann; Shak, Steven
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015730	A1	20010308	WO 2000-US23391	20000825 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2382100	AA	20010308	CA 2000-2382100	20000825 <--
BR 2000013814	A	20020423	BR 2000-13814	20000825 <--
EP 1210115	A1	20020605	EP 2000-959423	20000825 <--
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TR 200200472	T2	20020621	TR 2002-200200472	20000825 <--
JP 2003508447	T2	20030304	JP 2001-520142	20000825 <--
US 6627196	B1	20030930	US 2000-648067	20000825 <--
NZ 517150	A	20050128	NZ 2000-517150	20000825 <--
ZA 2002001229	A	20030416	ZA 2002-1229	20020213 <--
US 2004037824	A1	20040226	US 2003-600152	20030620 <--
PRIORITY APPLN. INFO.:			US 1999-151018P P	19990827 <--
			US 2000-213822P P	20000623 <--
			US 2000-648067 A3	20000825 <--
			WO 2000-US23391 W	20000825 <--

AB The present invention concerns the treatment of disorders characterized by the overexpression of ErbB2. More specifically, the invention concerns the treatment of human patients susceptible to or diagnosed with cancer overexpressing ErbB2 with anti-ErbB2 **antibody.**

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:824125 HCAPLUS
DOCUMENT NUMBER: 134:4050
TITLE: Treatment with anti-erbB2 **antibodies**
INVENTOR(S): Cohen, Robert L.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069460	A1	20001123	WO 2000-US12552	20000509 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

CA 2374085	AA	20001123	CA 2000-2374085		20000509 <--
EP 1187632	A1	20020320	EP 2000-928916		20000509 <--
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JP 2002544238	T2	20021224	JP 2000-617920		20000509 <--
AU 782325	B2	20050721	AU 2000-47080		20000509 <--
US 2003170235	A1	20030911	US 2003-429519		20030505 <--
PRIORITY APPLN. INFO.:			US 1999-134085P	P	19990514 <--
			US 2000-568322	A1	20000509 <--
			WO 2000-US12552	W	20000509 <--

AB A method treating a human patient to or diagnosed with a tumor in which erbB2 protein is expressed comprising the following steps, performed sequentially: (a) treating the patient with a therapeutically effective amount of an anti-erbB2 **antibody**; (b) surgically removing the tumor, and then (c) treating the patient with a therapeutically effective amount of an anti-erbB2 **antibody** or of a chemotherapeutic agent.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:68356 HCAPLUS
DOCUMENT NUMBER: 132:121460
TITLE: Methods and compositions for cancer treatment
INVENTOR(S): Marinkovich, Vincent
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000003733	A1	20000127	WO 1999-US15716		19990712 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9950970	A1	20000207	AU 1999-50970		19990712 <--
US 2003108555	A1	20030612	US 2001-764224		20010116 <--
PRIORITY APPLN. INFO.:			US 1998-93084P	P	19980716 <--
			WO 1999-US15716	W	19990712 <--

AB Compns., vaccines and kits for cancer immunotherapy are described. The compns., vaccines and kits may include transfer factor. The compns., vaccines and kits also include modified monoclonal **antibodies** directed to cancer cells, other specific cancer **receptor** agonists, or viruses which infect cancer cells. The invention is also directed to methods of cancer immunotherapy using the compns. and vaccines of the invention.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:405000 HCAPLUS
DOCUMENT NUMBER: 131:43591
TITLE: Combination therapy of cancer with anti-ErbB2 **antibodies**
INVENTOR(S): Shak, Steven; Paton, Virginia E.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9931140	A1	19990624	WO 1998-US26266		19981210	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
ZA 9811162	A	20000607	ZA 1998-11162		19981207	<--
CA 2311409	AA	19990624	CA 1998-2311409		19981210	<--
AU 9919081	A1	19990705	AU 1999-19081		19981210	<--
EP 1037926	A1	20000927	EP 1998-963840		19981210	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
TR 200001689	T2	20010122	TR 2000-200001689		19981210	<--
BR 9815363	A	20011016	BR 1998-15363		19981210	<--
JP 2002508397	T2	20020319	JP 2000-539062		19981210	<--
NZ 504597	A	20030530	NZ 2000-504597		20000517	<--
NO 2000002957	A	20000811	NO 2000-2957		20000609	<--
US 2003147884	A1	20030807	US 2003-356824		20030203	<--
US 2004037823	A9	20040226				
US 2003170234	A1	20030911	US 2003-406925		20030404	<--
US 2005002928	A1	20050106	US 2004-909998		20040802	<--
PRIORITY APPLN. INFO.:			US 1997-69346P	P	19971212	<--
			US 1998-208649	A3	19981210	<--
			US 1998-209023	A3	19981210	<--
			WO 1998-US26266	W	19981210	<--

AB The authors disclose the treatment of disorders characterized by the overexpression of ErbB2. More specifically, human patients are treated with a combination of an anti-ErbB2 **antibody** and a chemotherapeutic agent other than an anthracycline (e.g., doxorubicin or epirubicin). Preferably, the chemotherapeutic agent is Taxol.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L7             4 SEA FILE=REGISTRY ABB=ON  (PACLITAXEL OR GEMCITABINE OR
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L10         2070 SEA FILE=HCAPLUS ABB=ON  L9 AND ?RECEPT?
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L16  ANSWER 1 OF 2     MEDLINE on STN
ACCESSION NUMBER:   2004607491     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15581051
TITLE:              Herceptin and gemcitabine for
                    metastatic pancreatic cancers that
                    overexpress HER-2/neu.
AUTHOR:             Safran Howard; Iannitti David; Ramanathan Ramesh; Schwartz
                    Jonathan D; Steinhoff Margaret; Nauman Chris; Hesketh Paul;
                    Rathore Ritesh; Wolff Robert; Tantravahi Umadevi; Hughes T
                    Marilyn; Maia Chris; Pasquariello Terry; Goldstein Lisa;
                    King Thomas; Tsai James Y; Kennedy Teresa
CORPORATE SOURCE:   The Brown University Oncology Group, Providence, Rhode
                    Island, USA.. hsafran@lifespan.org
CONTRACT NUMBER:    2P30 CA47904 (NCI)
     5M01RR00056 (NCRR)
SOURCE:             Cancer investigation, (2004) 22 (5) 706-12.
                    Journal code: 8307154. ISSN: 0735-7907.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      (CLINICAL TRIAL)
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200412
ENTRY DATE:         Entered STN: 20041208
                    Last Updated on STN: 20041230
                    Entered Medline: 20041229
AB   PURPOSE: To determine the response rate and toxicities of
     Herceptin and gemcitabine for patients with metastatic
     pancreatic adenocarcinomas that overexpress HER
     -2/neu. METHODS AND MATERIALS: Patients with
     metastatic pancreatic cancer with 2+/3 + HER
     -2/neu expression by immunohistochemistry were
     eligible. Patients received gemcitabine, 1 g/m2/week, for 7 of
     8 weeks followed by 3 of every 4 weeks, and Herceptin, 4 mg/kg
     loading dose, followed by 2 mg/kg/week. RESULTS: Screening logs
     demonstrated the rate of HER-2/neu
     overexpression was 16%. Thirty-four patients were enrolled. Thirty
     patients (88%) had pancreatic cancers with 2+
     overexpression and 4 patients (12%) had 3+ overexpression. Toxicity was
     similar to gemcitabine alone. Confirmed partial responses were
     observed in 2 of 32 patients (6%). Thirteen of 32 patients (41%) had
     either a partial response or a >50% reduction in CA 19-9. The median
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survival for all 34 patients was 7 months, and the 1-year survival was 19%. CONCLUSION: The response rate of **Herceptin** and **gemcitabine** is similar to **gemcitabine** alone. The 7-month median survival in patients with metastatic **pancreatic cancer** suggests there may be a modest benefit for some patients. Infrequent **HER-2/neu** overexpression limits the role of targeting the **HER-2/neu** gene and prevents definitive conclusions on the addition of **Herceptin** to gemcibine for patients with **pancreatic cancer.**

L16 ANSWER 2 OF 2 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003250088 EMBASE
TITLE: Drug development in **pancreatic cancer**: Finally, biology begets therapy.
AUTHOR: Cohen S.J.; Meropol N.J.
CORPORATE SOURCE: Dr. N.J. Meropol, 7701 Burholme Avenue, Philadelphia, PA 19111, United States. NJ_Meropol@fccc.edu
SOURCE: International Journal of Gastrointestinal Cancer, (2002) Vol. 32, No. 2-3, pp. 91-106.
Refs: 130
ISSN: 0169-4197 CODEN: IJGCAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030710
Last Updated on STN: 20030710

AB **Pancreatic cancer** is rarely curable, and only 5% of patients achieve long-term survival. The vast majority of patients present with metastatic or unresectable disease. Standard chemotherapy with **gemcitabine** provides clinical benefit to only a small minority of patients. Thus, the development and investigation of new therapies is clearly needed. As knowledge of the underlying biology of **pancreatic cancer** has increased, targeted therapies based upon preclinical laboratory work have been developed, and are entering clinical trials. Some of these agents lack traditional dose-limiting toxicities (DLTs) at biologically active doses, and therefore clinical evaluation may not follow traditional guidelines for cytotoxic drug development. This article focuses on targeted therapies currently undergoing clinical evaluation in **pancreatic cancer.** Classes of therapeutics reviewed include those targeting tumor-microenvironment interactions (matrix metalloproteinase inhibitors, vascular endothelial growth-factor blockade), signal transduction (e.g., farnesyltransferase inhibitors), growth-factor **receptors** (epidermal growth-factor **receptor** blockade, **Her-2/neu**, gastrin), and vaccine approaches. Currently, there is a renewed optimism that the clinical application of biologic understanding will lead to an improved outcome for patients with **pancreatic cancer.**

```
=> d que stat l19
L5            1 SEA FILE=REGISTRY ABB=ON  HERCEPTIN/CN
L7            4 SEA FILE=REGISTRY ABB=ON  (PACLITAXEL OR GEMCITABINE OR
                5-FLUOROURACIL OR DOXORUBICIN)/CN
L9         2811 SEA FILE=HCAPLUS ABB=ON  (L5 OR ?HERCEPTIN? OR HER-2)
L10        2070 SEA FILE=HCAPLUS ABB=ON  L9 AND ?RECEPT?
L11         950 SEA FILE=HCAPLUS ABB=ON  L10 AND ?ANTIBOD?
L12         186 SEA FILE=HCAPLUS ABB=ON  L11 AND (L7 OR ?PACLITAXEL? OR
                ?GEMCITABINE? OR 5(W)?FLUOROURACIL? OR ?DOXORUBIXIN?)
L13          65 SEA FILE=HCAPLUS ABB=ON  L12 AND (?CANCER? OR ?CARCIN? OR
                ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)(3A)(?PANCR? OR ?COLON?)
L17         245 SEA FILE=USPATFULL ABB=ON  L13 AND HER(W)2(W)NEU
L18         152 SEA FILE=USPATFULL ABB=ON  L17 AND (PRD<20011207  OR PD<2001120
                7)
L19           2 SEA FILE=USPATFULL ABB=ON  L18 AND ?COMB?(W)?RADIAT?

=> d ibib abs l19 1-2

L19  ANSWER 1 OF 2  USPATFULL on STN
ACCESSION NUMBER:        2003:99203  USPATFULL
TITLE:                   Methods of treating neoplasia with combination of
                         target-cell specific adenovirus, chemotherapy and
                         radiation
INVENTOR(S):             Yu, De-Chao, Foster City, CA, UNITED STATES
                         Chen, Yu, Cupertino, CA, UNITED STATES
                         Henderson, Daniel R., Palo Alto, CA, UNITED STATES

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2003068307      A1   20030410
                         US 6911200         B2   20050628
APPLICATION INFO.:       US 2001-814357     A1   20010321  (9)

                                NUMBER         DATE
                         ------------------ --------
PRIORITY INFORMATION:    US 2000-192015P    20000324 (60)            <--
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    Debra J. Glaister, Morrison & Foerster LLP, 755 Page
                         Mill Road, Palo Alto, CA, 94304-1018
NUMBER OF CLAIMS:        58
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      42 Drawing Page(s)
LINE COUNT:              8142
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The invention provides methods of treating neoplasia using combinations
       of target cell-specific replication competent adenoviral vectors and
       chemotherapy, radiation therapy or combinations thereof. The adenoviral
       vectors are target cell-specific for the particular type of neoplasia
       for which treatment is necessary and the combination with the
       chemotherapy and/or radiation leads to synergistic treatment over
       existing adenoviral therapy or traditional chemotherapy and radiation
       therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19  ANSWER 2 OF 2  USPATFULL on STN
ACCESSION NUMBER:        2002:148271  USPATFULL
TITLE:                   Combination radiation therapy and
```

chemotherapy in conjunction with administration of growth factor **receptor antibody**

INVENTOR(S): Buchsbaum, Donald J., Birmingham, AL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002076408	A1	20020620
APPLICATION INFO.:	US 2001-4833	A1	20011207 (10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-251787P	20001208 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Hendricks and Associates, P. O. Box 2509, Fairfax, VA, 22031-2509
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 446
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention comprises a method of inhibiting tumor growth in tumors having growth factor **receptors** comprising administering, about simultaneously, **antibodies** to the target growth factor **receptors**, at least one chemotherapeutic agent and radiation therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d ibib abs ind l3 1-10

L3 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:151613 HCAPLUS
DOCUMENT NUMBER: 142:309420
TITLE: Combined ionizing **radiation** and sKDR gene delivery for treatment of prostate carcinomas
AUTHOR(S): Kaliberov, S. A.; Kaliberova, L. N.; **Buchsbaum, D. J.**
CORPORATE SOURCE: Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL, USA
SOURCE: Gene Therapy (2005), 12(5), 407-417
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Overexpression of vascular endothelial **growth factor** (VEGF) and its cognate receptor KDR has been linked to a more aggressive phenotype of human prostate carcinomas. The importance of signal transduction through the VEGF receptor 2 is illustrated by use of soluble KDR, which binds to VEGF and sequesters this ligand before its binding to cellular receptor. Treatment with recombinant adenovirus AdVEGF-sKDR, encoding sKDR under control of the human VEGF promoter, significantly inhibited the proliferation of human vascular endothelial cells and prostate cancer cells. AdVEGF-sKDR infection decreased migration of endothelial 1P-1B cells (61% reduction) and DU145 prostate carcinoma cells (47%) in comparison with AdCMV-Luc-infected control cells. Ionizing **radiation** upregulated VEGF promoter activity in prostate carcinoma and endothelial cells. AdVEGF-sKDR infection significantly reduced human vascular endothelial and prostate cancer cell proliferation and sensitized cancer cells to ionizing **radiation.** In vivo tumor therapy studies demonstrated significant inhibition of DU145 tumor growth in mice that received combined AdVEGF-sKDR infection and ionizing **radiation** vs. AdVEGF-sKDR alone or **radiation** therapy alone. These results suggest that selective transcriptional targeting of sKDR gene expression employing a **radiation** inducible promoter can effectively inhibit tumor growth and demonstrate the advantage of combination radiotherapy and gene therapy for the treatment of prostate cancer.
CC 1-6 (Pharmacology)
Section cross-reference(s): 3
ST ionizing **radiation** sKDR gene therapy prostate cancer VEGF
IT Gene therapy
Genetic vectors
Human
Ionizing **radiation**
Prostate gland, neoplasm
Radiotherapy
(combined ionizing **radiation** and sKDR gene delivery for treatment of prostate carcinomas)
IT Promoter (genetic element)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combined ionizing **radiation** and sKDR gene delivery for treatment of prostate carcinomas)
IT Blood vessel
(endothelium; combined ionizing **radiation** and sKDR gene delivery for treatment of prostate carcinomas)
IT Vascular endothelial **growth factor** receptors
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type VEGFR-2; combined ionizing **radiation** and sKDR gene delivery for treatment of prostate carcinomas)
IT Endothelium
(vascular; combined ionizing **radiation** and sKDR gene delivery for treatment of prostate carcinomas)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1004497 HCAPLUS
DOCUMENT NUMBER: 142:106783
TITLE: Adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer
AUTHOR(S): Kaliberov, Sergey A.; Kaliberova, Lyudmila N.; Stockard, Cecil R.; Grizzle, William E.; **Buchsbaum, Donald J.**
CORPORATE SOURCE: Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Molecular Therapy (2004), 10(6), 1059-1070
CODEN: MTOHCK; ISSN: 1525-0016
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL/Apo2L) is of particular interest in the development of prostate carcinoma therapeutics as it preferentially induces apoptosis of tumor cells. To employ adenoviral vectors for highly efficient and specific TRAIL gene transfer into cancer cells could overcome some potential problems for recombinant TRAIL. The vascular endothelial **growth factor** receptor FLT-1 is involved in regulation of angiogenesis and tumor growth, invasion, and metastasis of prostate carcinoma. FLT-1 expression is observed in both tumor endothelial cells and prostate cancer cells. We developed an adenoviral vector encoding the TRAIL gene under control of the FLT1 promoter (AdFlt-TRAIL), which produced endothelial and prostate cancer cell death. The combination of ionizing **radiation** and adenovirus-driven TRAIL expression overcame human prostate cancer cell resistance to TRAIL. Furthermore, in vivo administration of AdFlt-TRAIL at the site of tumor growth in combination with **radiation** treatment produced significant suppression of the growth of DU145 human prostate tumor xenografts in athymic nude mice. Our results suggest that specific TRAIL delivery employing the FLT1 promoter can effectively inhibit tumor growth and demonstrate the advantage of combination radiotherapy and gene therapy for the treatment of prostate cancer.
CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 8
ST antiangiogenesis gene therapy prostate cancer TRAIL radiotherapy flt1 adenovirus
IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand); adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer)
IT Angiogenesis inhibitors
Antitumor agents
Apoptosis
Gene therapy
Genetic vectors

Human
Human adenovirus
Radiotherapy
(adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer)

IT Promoter (genetic element)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer)

IT Prostate gland, neoplasm
(carcinoma; adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer)

IT Vascular endothelial **growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene, flt 1; adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer)

IT Carcinoma
(prostatic; adenovirus-mediated FLT1-targeted proapoptotic gene therapy of human prostate cancer)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:404840 HCAPLUS
DOCUMENT NUMBER: 142:129837
TITLE: Anti-EGFR-mediated radiosensitization as a result of augmented EGFR expression
AUTHOR(S): Bonner, James A.; **Buchsbaum, Donald J.**; Russo, Suzanne M.; Fiveash, John B.; Trummell, Hoa Q.; Curiel, David T.; Raisch, Kevin P.
CORPORATE SOURCE: Department of Radiation Oncology, Univ. Alabama Sch Med., Birmingham, AL, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2004), 59(2, Suppl.), 2-10
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Elevated epidermal **growth factor** receptor (EGFR) expression has correlated with a poor prognosis after standard treatment of several malignancies. However, it is not clear whether the absolute level of EGFR expression affects the radiosensitizing properties of anti-EGFR treatments. A better understanding of this question would be helpful for the design of protocols that deliver these treatments. To explore this question, cells (LS174T) that did not display inherent anti-EGFR treatment-induced radiosensitization were selected for studies that could potentially enhance EGFR expression. Human colon carcinoma cells (LS174T), which did not show radiosensitization by anti-EGFR treatments, were employed for these studies. (Also, these cells were not responsive to the antiproliferative effects of anti-EGFR treatment.). Using standard transfection techniques (eukaryotic expression vector) as well as an adenoviral construct to enhance EGFR expression, LS174T cells were transduced in a manner that resulted in enhanced expression of EGFR. Subsequently, standard proliferation studies were performed to test the radiosensitizing properties of anti-EGFR treatment (an anti-EGFR monoclonal antibody: IMC-C225). Studies were undertaken to stably transfect LS174T cells with EGFR. The stable transfectants, LS174T.EGFR cells, were responsive to the antiproliferative effects of anti-EGFR treatment, in contrast to the parent LS174T cells. Similar results were

demonstrated when the cells were infected with AdEGFR. Addnl., the LS174T.EGFR cells were responsive to the radiosensitizing properties of anti-EGFR treatment (IMC-C225), whereas the parent cells were not. Although the level of EGFR expression is of prognostic significance in many tumor models, the response of cells to anti-EGFR treatment alone, or combinations of this treatment with **radiation** or chemotherapy, depends upon many factors that are not necessarily related to the inherent EGFR expression of the tumor cells. However, the studies reported herein, demonstrate that when LS174T cells were transduced to show increased EGFR expression, they became responsive to the radiosensitizing properties of anti-EGFR treatments.

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1

ST EGFR antibody radiosensitizer radiotherapy

IT Adenoviral vectors
(AdEGFR; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERBB1; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Chemotherapy
Human
Radiosensitizers, biological
Transformation, genetic
(anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Epidermal **growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Intestine, neoplasm
(colon, carcinoma; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Carcinoma
(colon; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Cell proliferation
(inhibition; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, iodo, labeled with iodine-125, IMC-C225, anti-EGFR; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

IT Radiotherapy
(targeted; anti-EGFR-mediated radiosensitization as result of augmented EGFR expression)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:523030 HCAPLUS
DOCUMENT NUMBER: 140:35435
TITLE: Differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody
AUTHOR(S): Huang, Zhi-qiang; **Buchsbaum, Donald J.**;

Raisch, Kevin P.; Bonner, James A.; Bland, Kirby I.; Vickers, Selwyn M.
CORPORATE SOURCE: Department of Radiation Oncology, Department of Surgery and Division of Radiation Biology, Division of General Surgery, University of Alabama at Birmingham, Birmingham, AL, USA
SOURCE: Journal of Surgical Research (2003), 111(2), 274-283
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background. Pancreatic cancer remains a devastating disease, with 95% of all patients diagnosed with the disease dying within 2 yr. The combined therapy using Erbitux, gemcitabine, and **radiation** caused complete tumor regression using a nude mouse model inoculated with pancreatic MiaPaCa-2 cells but only a delay in tumor growth with BxPC-3. We investigated the effect of prolonged Erbitux treatment to the sensitivity to gemcitabine and/or **radiation** and the epidermal **growth factor** receptor (EGFR) signal transduction pathway. MiaPaCa-2 and BxPC-3 cells were cultured with or without Erbitux for 6 wk. Cells were then treated with gemcitabine and/or **radiation**, harvested 48 h after treatment, and counted. Differences in EGFR expression after exposure to Erbitux were analyzed by FACS. Internalization rates of EGFR induced by Erbitux on these cell lines were determined using 125I-EGF binding assay after removal of Erbitux by acidic wash. Cell lysates were harvested after cells were stimulated with EGF, FGF, or IGF-1 resp., and EGFR was immunopptd. using Erbitux. Samples were separated using SDS-PAGE and transferred to PVDF membrane. The membranes were probed with antibody against human **growth factor** receptor binding protein (Grb2) to detect the association of this Ras-MAPK upstream adaptor protein to EGFR. Cell lysates were also separated with SDS-PAGE and probed with rabbit anti-human PARP after samples were transferred to PVDF membrane. Expression of BAX and Bcl-XL were probed in the cells treated with or without Erbitux. Proliferation assays indicated that prolonged exposure to Erbitux increased the sensitivities of MiaPaCa-2 to gemcitabine and **radiation** therapy (41±16% vs. 52±9% for gemcitation, 28±9 vs. 39±9% for combination; P = 0.015) but not for BxPC-3. FACS anal. showed that the expressed EGFR level decreased by about 42% on MiaPaCa 2 whereas no loss was seen on BxPC-3. Expression of BAX was upregulated on MiaPaCa-2. Poly (ADP-ribose) polymerase cleavage indicated the killing was mediated by apoptosis. Immunoblots showed that Grb2 was co-immunopptd. with EGFR after EGF stimulation. Incubation with Erbitux blocked Grb2 binding in MiaPaCa-2 but not BxPC 3. FGF transactivated EGFR down stream Ras-MAPK in the presence or absence of Erbitux. Internalization of EGFR induced by Erbitux did not differ between MiaPaCa-2 and BxPC-3. Conclusions. (1) Association of Grb2 to EGFR in BxPC-3 induced by EGF in the presence of Erbitux indicates an alternate pathway of Ras-MAPK activation, which may be related with the tumor resistance to treatment; (2) transactivation of EGFR downstream Ras-MAPK pathway by FGF contributes the resistance to treatment; and (3) downregulation of EGFR may increase the response to therapy.
CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 15
ST pancreas carcinoma Erbitux EGFR antibody
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bcl-xL; differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GRB-2 (**growth factor** receptor-bound protein 2); differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Drug resistance
(antitumor; differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Pancreas, neoplasm
(carcinoma; differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Antitumor agents
Apoptosis
Drug interactions
Human
Radiotherapy
Signal transduction, biological
(differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Epidermal **growth factor** receptors
Ras proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Biological transport
(internalization; differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT Carcinoma
(pancreatic; differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT 142243-02-5, MAPK
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
IT 95058-81-4, Gemcitabine 205923-56-4, Erbitux
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential responses by pancreatic carcinoma cell lines to prolonged exposure to Erbitux (IMC-C225) anti-EGFR antibody)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:839606 HCAPLUS
DOCUMENT NUMBER: 139:32573
TITLE: Treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**
AUTHOR(S): **Buchsbaum, Donald J.**; Bonner, James A.; Grizzle, William E.; Stackhouse, Murray A.; Carpenter,

Mark; Hicklin, Daniel J.; Bohlen, Peter; Raisch, Kevin P.
CORPORATE SOURCE: Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2002), 54(4), 1180-1193
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: To investigate treatment of human pancreatic cancer cell lines and xenografts with combinations of Erbitux (IMC-C225) anti-epidermal **growth factor** receptor (EGFR) antibody, gemcitabine, and **radiation.** Methods and Materials: BxPC-3 and MiaPaCa-2 human pancreatic carcinoma cells were treated in vitro for 24 h with IMC-C225 (5 μg/mL), then exposed to epidermal **growth factor** (EGF) (10 mM) for 5 min. Immunoblots were screened for EGFR expression and the ability of IMC-C225 to block EGF-induced tyrosine phosphorylation of EGFR. Cells were treated with IMC-C225 (5 μg/mL) on Day 0, the IC50 dose of gemcitabine on Day 1 for 24 h, followed by 3 Gy 60Co irradiation on Day 2, or the combination of each agent. For cell proliferation, cells were counted on Day 4, and for apoptosis, cells were stained with annexin V-FITC and propidium iodide, then analyzed by FACS. Cells were treated with the same single or multiple treatments and analyzed in a clonogenic cell survival assay. The effect of IMC-C225, gemcitabine, and **radiation** on the growth of BxPC-3 and MiaPaCa-2 tumor xenografts was determined Athymic nude mice bearing established s.c. tumor xenografts of 6-8 mm diameter received 6 wk of treatment with IMC-C225 (1 mg every 3 days + 6) alone or in combination with gemcitabine (120 mg/kg i.v. every 6 days + 6), and 6 weekly fractions of 3 Gy **radiation** on the days after gemcitabine administration. Tumor growth was measured with Vernier calipers. Results: BxPC-3 and MiaPaCa-2 cell lines expressed low levels of EGFR. IMC-C225 inhibited EGF-induced tyrosine phosphorylation of the EGF receptor on both cell lines. Treatment of cells with a combination of IMC-C225 + gemcitabine + **radiation** produced the highest induction of apoptosis and inhibition of proliferation in vitro. Combination treatment with IMC-C225, gemcitabine, and **radiation** produced 100% complete regression of MiaPaCa-2 tumors for more than 250 days, and the greatest growth inhibition of BxPC-3 tumors compared to any single or dual treatments. Conclusions: The IMC-C225 therapy in combination with gemcitabine chemotherapy and **radiation** therapy demonstrated statistically significantly greater efficacy over the single and double combination therapies. This form of multimodality treatment shows potential clin. application in the treatment of pancreatic cancer in humans.
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1
ST pancreas carcinoma Erbitux EGFR antibody gemcitabine radiotherapy
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-EGFR; treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT Pancreas, neoplasm
(carcinoma; treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT Carcinoma
(pancreatic; treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)

IT Drug interactions
(pharmacodynamic; treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT Antitumor agents
Apoptosis
Cell proliferation
Chemotherapy
Human
Phosphorylation, biological
Radiosensitizers, biological
Radiotherapy
(treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT Epidermal **growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT 62229-50-9, Epidermal **growth factor** 79079-06-4, EGFR
Tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT 205923-56-4, Erbitux
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
IT 95058-81-4, Gemcitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of pancreatic cancer xenografts with Erbitux (IMC-C225) anti-EGFR antibody, gemcitabine, and **radiation**)
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:449450 HCAPLUS
DOCUMENT NUMBER: 137:706
TITLE: Combination **radiation** therapy and chemotherapy in conjunction with administration of **growth factor** receptor antibody
INVENTOR(S): **Buchsbaum, Donald J.**
PATENT ASSIGNEE(S): UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002045653	A2	20020613	WO 2001-US46179	20011207
WO 2002045653	A3	20030103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002039486	A5	20020618	AU 2002-39486		20011207
US 2002076408	A1	20020620	US 2001-4833		20011207
PRIORITY APPLN. INFO.:			US 2000-251787P	P	20001208
			WO 2001-US46179	W	20011207

AB The invention comprises a method of inhibiting tumor growth in tumors having **growth factor** receptors comprising administering, about simultaneously, antibodies to the target **growth factor** receptors, at least one chemotherapeutic agent, and **radiation** therapy.

IC ICM A61K

CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 15

ST chemotherapeutic radiotherapy **growth factor** receptor antibody combination tumor treatment

IT Antitumor agents
Apoptosis
Chemotherapy
Drug interactions
Human
Pancreas, neoplasm
Radiotherapy
(chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT Epidermal **growth factor** receptors
Growth factor receptors
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT Intestine, neoplasm
(colon; chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT Neoplasm
(epidermoid; chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT 205923-56-4, IMC-C 225
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IMC-C 225; chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT 79079-06-4, EGF receptor tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

IT 51-21-8, 5-Fluorouracil 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 100286-90-6, CPT-11 180288-69-1, Herceptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chemotherapy combination with radiotherapy and **growth factor** receptor antibody for tumor treatment)

L3 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:581735 HCAPLUS
DOCUMENT NUMBER: 135:151638
TITLE: Enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies
INVENTOR(S): **Buchsbaum, Donald J.**; Curiel, David T.; Stackhouse, Murray
PATENT ASSIGNEE(S): Uab Research Foundation, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001056604	A1	20010809	WO 2001-US3949		20010207
W: AU, CA, JP					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
US 6468547	B1	20021022	US 2000-499543		20000207
PRIORITY APPLN. INFO.:			US 2000-499543	A	20000207
			US 1996-29673P	P	19961030
			US 1997-961327	A2	19971030

AB The present invention provides a method of enhancing the chemosensitivity and radiosensitivity of a neoplastic cell expressing an oncoprotein that stimulates proliferation of the cell, comprising introducing into the cell a nucleic acid mol. encoding an antibody homolog, wherein the antibody homolog is expressed intracellularly and binds to the oncoprotein intracellularly in the endoplasmic reticulum of the cell. The present invention is also directed to a method for enhancing the inhibition of proliferation of a neoplastic cell expressing an oncoprotein that stimulates proliferation of the cell, comprising the steps of: introducing into the cell a nucleic acid mol. encoding an antibody homolog, wherein the antibody homolog is expressed intracellularly and binds to the protein intracellularly; and contacting said cell with an anti-neoplastic agent.
IC ICM A61K039-395
ICS A61K048-00; C12N015-09; C12N015-13
CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 8, 14
ST tumor chemosensitivity radiosensitivity single chain antibody
IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BAG-1; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Adenoviridae
(C6.5; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(D1; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bcl-2; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Uterus, neoplasm
(cervix; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Intestine, neoplasm
(colon; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Antitumor agents
Chemotherapy
Leukemia
Lung, neoplasm
Melanoma
Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Radiotherapy
Sarcoma
(enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Apoptosis
Cell cycle
Cell proliferation
DNA sequences
Plasmid vectors
Radiation
Transformation, genetic
Virus vectors
(enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT DNA
Gene, animal
Nucleoside analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Epidermal **growth factor** receptors
Growth factor receptors
Transforming proteins
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Sarcoma
(fibrosarcoma; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments, Fab; single-chain; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments, Fv; single-chain; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Neuroglia
(glioma; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
IT Bladder
Digestive tract
Mammary gland
Prostate gland
Salivary gland
(neoplasm; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Bone, neoplasm
(osteosarcoma; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Kidney, neoplasm
(renal cell carcinoma; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Eye, neoplasm
(retinoblastoma; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(single chain; enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies)
IT 51-21-8, 5-fluorouracil 127-07-1, hydroxyurea 154-93-8, bcnu 289-95-2D, pyrimidine, fluoro derivs. 289-95-2D, pyrimidine, halogenated derivs. 1404-00-8, mitomycin 11056-06-7, bleomycin 15663-27-1, cisplatin 21679-14-1, fludarabine 33069-62-4, taxol 33419-42-0, etoposide 143180-75-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of tumor cell chemosensitivity and radiosensitivity using single chain secretory antibodies in relation to)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:822458 HCAPLUS
DOCUMENT NUMBER: 135:16104
TITLE: Enhanced apoptosis with combination C225/ **radiation** treatment serves as the impetus for clinical investigation in head and neck cancers
AUTHOR(S): Bonner, James A.; Raisch, Kevin P.; Trummell, Hoa Q.;

Robert, Francisco; Meredith, Ruby F.; Spencer, Sharon A.; **Buchsbaum, Donald J.**; Saleh, Mansoor N.; Stackhouse, Murray A.; LoBuglio, Albert F.; Peters, Glenn E.; Carroll, William R.; Waksal, Harlan W.
CORPORATE SOURCE: Comprehensive Cancer Center (Experimental Therapeutics Program), University of Alabama at Birmingham, Birmingham, AL, 35294-3300, USA
SOURCE: Journal of Clinical Oncology (2000), 18(21, Suppl.), 47S-53S
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epidermal **growth factor** receptor (EGFr) is overexpressed in a majority of head and neck squamous cell carcinomas, and this overexpression is associated with a poor prognosis. Therefore, EGFr has become the target of investigations aimed at disabling the receptor to determine whether this process leads to improved tumor kill with conventional treatment. C225 is an anti-EGFr monoclonal antibody that inhibits receptor activity by blocking the ligand binding site. A panel of human head and neck squamous cell carcinoma cell lines was used to study the combination of C225 and **radiation.** It was determined that the combination of C225 (5 μg/mL) delivered simultaneously with **radiation** (3 Gy) resulted in a greater decrement in cellular proliferation than either treatment alone. This reduction in proliferation correlated with reduced EGFr tyrosine phosphorylation and a reduction in phosphorylated signal transducer and activator of transcription-3 (STAT-3) protein (known to protect cells from apoptosis). Also, the decrement in proliferation correlated with increased apoptotic events, thereby indirectly linking C225/**radiation**-induced regulation of STAT-3 protein to apoptosis. This preclin. work serves as important support for the ongoing clin. investigation of C225 and radiotherapy for patients with head and neck carcinomas. The initial results of these clin. studies have been promising.
CC 8-9 (Radiation Biochemistry)
ST head neck squamous carcinoma radiotherapy antiEGFr antibody; epidermal **growth factor** receptor squamous carcinoma radiotherapy
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(STAT3; effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)
IT Apoptosis
Radiotherapy
(effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)
IT Epidermal **growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)
IT Antitumor agents
(head and neck squamous cell carcinoma; effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, C225; effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)

IT Head
Neck, anatomical
(squamous cell carcinoma, inhibitors; effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)
IT Head
Neck, anatomical
(squamous cell carcinoma; effect of combined radiotherapy and anti-EGFr monoclonal antibody on head and neck cancers)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:29947 HCAPLUS
DOCUMENT NUMBER: 132:290547
TITLE: Combined modality therapy of A431 human epidermoid cancer using anti-EGFr antibody C225 and **radiation**
AUTHOR(S): Saleh, Mansoor N.; Raisch, Kevin P.; Stackhouse, Murray A.; Grizzle, William E.; Bonner, James A.; Mayo, Matthew S.; Kim, Hyung-Gyoon; Meredith, Ruby F.; Wheeler, Richard H.; **Buchsbaum, Donald J.**
CORPORATE SOURCE: Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Cancer Biotherapy & Radiopharmaceuticals (1999), 14(6), 451-463
CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background. Monoclonal antibodies (mAb) to epidermal **growth factor** receptor (EGFr) inhibit tumor cell proliferation and enhance cytotoxicity of chemotherapeutic agents. The purpose of this study was to investigate the interaction of the anti-EGFr antibody C225 combined with radiotherapy (RT) on EGFr expressing A431 human epidermoid cancer cells. Methods. Cell proliferation, apoptosis, EGFr expression and phosphorylation, and clonogenic survival were assayed in vitro. A431 tumor growth inhibition and immunohistochem. anal. of EGFr expression and apoptosis were assessed in vivo. Results. C225 plus RT produced greater inhibition of A431 cell proliferation than C225 or RT alone which was corroborated by enhanced apoptosis. Similar clonogenic survival occurred following the addition of C225 to RT, although colonies were smaller in the presence of C225. C225 produced inhibition of EGF-induced phosphorylation of EGFr without concurrent down-regulation of surface receptor, which was not altered by RT. Combined treatment of mice bearing tumors demonstrated enhancement of complete regressions, reduction in time to tumor size doubling, and prolongation of survival. Significant apoptosis occurred in xenograft tumors treated with C225 with or without RT. Conclusions. These data demonstrate an interaction between C225 and RT. C225-mediated apoptosis and inhibition of EGFr phosphorylation may be critical in the interaction. Studies to define the precise influence of combined modality treatment on the EGFr signal transduction cascade need to be pursued. The combination of **growth factor** receptor antibodies and RT has potential application in clin. oncol.
CC 8-9 (Radiation Biochemistry)
ST epidermoid cancer radiotherapy antiEGFr antibody
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chimeric; combined modality therapy of A431 human epidermoid cancer using anti-EGFr antibody C225 and **radiation**)
IT Radiotherapy
(combined modality therapy of A431 human epidermoid cancer using anti-EGFr antibody C225 and **radiation**)
IT Epidermal **growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combined modality therapy of A431 human epidermoid cancer using anti-EGFr antibody C225 and **radiation**)
IT Antitumor agents
(squamous cell carcinoma; combined modality therapy of A431 human epidermoid cancer using anti-EGFr antibody C225 and **radiation**)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:753259 HCAPLUS
DOCUMENT NUMBER: 132:2792
TITLE: Treatment of human tumors with **radiation** and antibodies to **growth factor** receptor kinases
INVENTOR(S): Waksal, Harlan W.; Saleh, Mansoor N.; Robert, Francisco; **Buchsbaum, Donald Jay**
PATENT ASSIGNEE(S): Imclone Systems Incorporated, USA; UAB Research Foundation
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9960023	A1	19991125	WO 1999-US10741		19990514
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2332331	AA	19991125	CA 1999-2332331		19990514
AU 9940799	A1	19991206	AU 1999-40799		19990514
EP 1080113	A1	20010307	EP 1999-924253		19990514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
BR 9910511	A	20011120	BR 1999-10511		19990514
JP 2002515511	T2	20020528	JP 2000-549641		19990514
ZA 2000007412	A	20020312	ZA 2000-7412		20001212
US 2004057950	A1	20040325	US 2003-661881		20030911
PRIORITY APPLN. INFO.:			US 1998-79612	A	19980515
			US 1998-85613P	P	19980515
			US 1998-206138	A	19981207
			US 1999-312286	B3	19990514
			WO 1999-US10741	W	19990514

AB The authors disclose a treatment regimen to inhibit the growth of tumors in human patients. The regimen comprises the co-administration of **radiation** and a non-radiolabeled protein receptor tyrosine kinase inhibitor (e.g., monoclonal antibodies). In one example, human patients were treated with anti-EGF receptor chimeric antibody c225 along with external beam **radiation.**

IC ICM C07K016-00
ICS A61K039-395

CC 15-3 (Immunochemistry)
Section cross-reference(s): 2, 8, 14

ST antitumor **radiation** receptor tyrosine kinase inhibitor

IT Antitumor agents
(bladder; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)

IT Antitumor agents
Antitumor agents
(brain; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric; to **growth factor** receptor tyrosine kinases for combination therapy of human tumors)

IT Intestine, neoplasm
Intestine, neoplasm
(colon, inhibitors; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)

IT Antitumor agents
(colon; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)

IT Antitumor agents
(combination therapy of **radiation** and inhibitors of **growth factor** receptor tyrosine kinases as)

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments, hypervariable region; to **growth factor** receptor tyrosine kinases for combination therapy of human tumors)

IT Antitumor agents
(head; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)

IT **Growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(heregulin, ErbB-3; tumor therapy with **radiation** and antibodies to)

IT **Growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(heregulin, ErbB-4; tumor therapy with **radiation** and antibodies to)

IT **Growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heregulin, ErbB-4; tumor therapy with **radiation** and antibodies to)

IT **Growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(heregulin, erbB-3; tumor therapy with **radiation** and antibodies to)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized; to **growth factor** receptor tyrosine

kinases for combination therapy of human tumors)
IT Radiotherapy
(in combination with inhibitors of **growth factor** receptor tyrosine kinases for tumor therapy)
IT Brain, neoplasm
Brain, neoplasm
Kidney, neoplasm
Kidney, neoplasm
Lung, neoplasm
Lung, neoplasm
Ovary, neoplasm
Ovary, neoplasm
(inhibitors; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Antitumor agents
Antitumor agents
(kidney; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Antitumor agents
Antitumor agents
(lung; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Antitumor agents
(mammary gland; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; to **growth factor** receptor tyrosine kinases for combination therapy of human tumors)
IT Antitumor agents
(neck; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Bladder
Bladder
Head
Head
Mammary gland
Mammary gland
Neck, anatomical
Neck, anatomical
Prostate gland
Prostate gland
(neoplasm, inhibitors; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Antitumor agents
Antitumor agents
(ovary; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Antitumor agents
(prostate gland; combination therapy with **radiation** and antibodies to **growth factor** receptor tyrosine kinases as)
IT Phosphorylation, biological
(protein; of EGF receptor is inhibited by monoclonal antibodies in relation to combination therapy of human tumors)
IT Epidermal **growth factor** receptors

Insulin-like **growth factor** I receptors
Nerve **growth factor** receptors
Transforming **growth factor** receptors
neu (receptor)
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(tumor therapy with **radiation** and antibodies to)

IT **Growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(tumor therapy with **radiation** and inhibitors of)

IT Fibroblast **growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(type 1; tumor therapy with **radiation** and antibodies to)

IT Fibroblast **growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(type 2; tumor therapy with **radiation** and antibodies to)

IT Fibroblast **growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(type 3; tumor therapy with **radiation** and antibodies to)

IT Fibroblast **growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(type 4; tumor therapy with **radiation** and antibodies to)

IT Platelet-derived **growth factor** receptors
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(α; tumor therapy with **radiation** and antibodies to)

IT 250741-11-8, PN: WO9960023 SEQID: 5 unclaimed DNA
RL: PRP (Properties)
(Unclaimed; treatment of human tumors with **radiation** and antibodies to **growth factor** receptor kinases)

IT 79079-06-4, EGF receptor tyrosine kinase 136396-12-8, Platelet-derived **growth factor** receptor β tyrosine kinase
137010-36-7, NGF receptor tyrosine kinase 137632-09-8 147014-95-7, C-ErbB-3 protein kinase 150027-15-9, Fibroblast **growth factor** receptor 1 tyrosine kinase 150027-21-7, Platelet-derived **growth factor** receptor α tyrosine kinase
150316-06-6, FGF receptor kinase type 2
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(tumor therapy with **radiation** and antibodies to)

IT 127407-08-3, Receptor tyrosine kinase
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(tumor therapy with **radiation** and inhibitors of)

IT 250741-00-5, 1: PN: WO9960023 SEQID: 1 unclaimed DNA 250741-10-7, 2: PN: WO9960023 SEQID: 3 unclaimed DNA 250741-12-9, 3: PN: WO9960023 SEQID: 7 unclaimed DNA 250741-14-1, 4: PN: WO9960023 SEQID: 9 unclaimed DNA
250741-17-4, 5: PN: WO9960023 SEQID: 11 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; treatment of human tumors with **radiation** and antibodies to **growth factor** receptor kinases)

IT 155661-31-7 186759-74-0
RL: PRP (Properties)
(unclaimed protein sequence; treatment of human tumors with **radiation** and antibodies to **growth factor** receptor kinases)

IT 250718-27-5 250718-28-6 250718-29-7 250718-31-1
RL: PRP (Properties)
(unclaimed sequence; treatment of human tumors with **radiation** and antibodies to **growth factor** receptor kinases)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT